

G. Jomer

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DDDDD  II  AAAAAA  LL      OOOOO  GGGGG
DD      DD II AA      AA LL      OO      OOGG      GG
DD      DD II AA      AA LL      OO      OG
DD      DD II AA AAAAAAALL      OO      OG      GGGG
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DD DDDD  II AA      AA LLLLLLLOOOOOOOO  GGGGGGG
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Dialog Information Services, Incorporated

ATTN: KATHLEEN FULLER

NOTE: SEARCH DONE COURTESY OF STIC-BIOTECH/CHEM LIBRARY

File(s) searched:

File 351: Derwent WPI 1981-1994/UD-9420;UA-9417UM-9409  
 (c) 1994 Derwent Info Ltd  
 File 350: Derwent World Pat 1963-1980/UD-9416  
 (c) 1994 Derwent Info Ltd

Sets selected:

Set	Items	Description
1	169	THROMBOPLASTIN?
2	62	PROTHROMBIN() TIME
3	38	S1 AND S2
4	145808	DRY
5	2	S3 AND S4
6	8	RECOMBINANT() TISSUE
7	0	S3 AND S6
8	0	RECOMBINANT PROTEINS! FROM155
9	284	RECOMBINANT() PROTEIN? ?
10	0	S10
11	0	S12
12	19	DIAGNOSIS/DE
13	0	(S10 OR S12) AND DIAGNOSIS/DE
14	159348	STRIP
15	0	S3 AND STRIP
16	145220	TEST
17	16	S3 AND TEST
18	0	S19
19	8388	ASSAY?
20	0	S19 AND ASSAY?
21	6322	RECOMBINANT
22	0	S3 AND RECOMBINANT
23	2	3 AND 19
24	196410	SOLID
25	0	S3 AND SOLID
26	224173	SUBSTRATE
27	3	S3 AND SUBSTRATE
28	7	5 OR 23 OR 27
29	64509	MEMBRANE
30	1	S3 AND MEMBRANE
31	953	CLOTTING
32	836	COA
33	32	S1 AND (CLOTTING OR COA)
34	953	CLOTTING
35	20097	COAGULAT?
36	113	S1 AND (CLOTTING OR COAGULAT?)
37	22	36 AND (4 OR 14 OR 24 OR 26 OR 29)
38	25	28 OR 37 OR 30

Prints requested : ('\*' indicates user print cancellation)

Date	Time	Description
20jul	11:47EST	P222: PR 38/7/ALL VIA MODEM (items 1-25 ADDR ADDEPTA)

Record - 1

DIALOG(R) File 351:Derwent WPI  
(c) 1994 Derwent Info Ltd. All rts. reserv.

009817188 WPI Acc No: 94-097044/12  
XRAM Acc No: C94-044237  
XRPX Acc No: N94-076263

Dry reagent for measurement of blood coagulation time - contains partial thromboplastin, ellagic acid, calcium chloride and magnetic particles

Patent Assignee: (TOKU ) TOKUYAMA SODA KK

Number of Patents: 001

Number of Countries: 001

Patent Family:

CC Number	Kind	Date	Week	
JP 6046897	A	940222	9412	(Basic)

Priority Data (CC No Date): JP 92198487 (920724)

Abstract (Basic): JP 06046897 A

A dry reagent for the measurement of blood coagulation time contains a partial thromboplastic, ellagic acid (EA), Ca chloride and magnetic particles.

USE/ADVANTAGE - The reagent can distinguish normality and abnormality in the internally caused blood coagulation activity and shows a clearer end point than that shown by the conventional reagent.

In an example, an activated partial thromboplastic time (APTT) reagent soln. using EA as the activator and 30 mM aq. Ca chloride soln. were mixed together at a ratio of 1:1. Tween 80 was added to the mixt. to a final concn. of 0.015%. Magnetic particles were suspended in it to a final concn. of 5 mg/ml to give a soln. for the dry APTT reagent. 25 micro-l of it was fractionated to a reaction slide. The slide was frozen instantaneously with liq. nitrogen to give a dry reagent for APTT determination. The reagent was set in an APTT measuring equipment and 25 micro-l of human serum was added and the motion signal of the magnetic particles was monitored optically. The decrease in the signal intensity was more significant than when a conventional APTT reagent was used. Dwg.0/6

Derwent Class: B04; D16; S03;

Int Pat Class: C12Q-001/56; G01N-033/86

Record - 2

DIALOG(R) File 351:Derwent WPI  
(c) 1994 Derwent Info Ltd. All rts. reserv.

009814996 WPI Acc No: 94-094852/12  
XRAM Acc No: C94-043359  
XRPX Acc No: N94-074291

Dry reagent for blood coagulation time measurement - comprises thromboplastin, activation agent, calcium chloride, detergent and magnetic particles

Patent Assignee: (TOKU ) TOKUYAMA SODA KK

Number of Patents: 001

Number of Countries: 001

Patent Family:

CC Number	Kind	Date	Week	
JP 6038797	A	940215	9412	(Basic)

(cont. next page)

Priority Data (CC No Date): JP 92197076 (920723)

Abstract (Basic): JP 06038797 A

Dry reagent for coagulation time measurement contains a part of thromboplastic, activation agent, CaCl<sub>2</sub>, detergent and magnetic particles.

USE/ADVANTAGE - Detection of the end of coagulation is easy because the plasma is quickly solved by the addn. of the detergent.

In an example, 14 mg of Fe<sub>3</sub>O<sub>4</sub> was added to 1.4 ml of APTT reagent soln. (A). 0.1 w/v% Triton X-100 was added to 1.4 ml of 20 mM CaCl<sub>2</sub> (B). A and B were mixed and 20 micro-litres of the soln. was dropped into the reaction cell. It was dried at (-80) deg.C for 1 day and then (-30) to 20 deg.C for 7 hours. The dry reagent was obtd. 25 ml of plasma was added to the dry reagent and analysed using CG01.

Dwg.0/4

Derwent Class: B04; D16; S03;

Int Pat Class: C12Q-001/56; G01N-033/86

### Record - 3

DIALOG(R)File 351:Derwent WPI

(c) 1994 Derwent Info Ltd. All rts. reserv.

009802981 WPI Acc No: 94-082835/10

XRAM Acc No: C94-037898

Peptides based on platelet factor 4 - used for neutralising the coagulant effects of heparin, partic. after administration of heparin

Patent Assignee: (REPK ) REPLIGEN CORP

Author (Inventor): BOYD J

Number of Patents: 001

Number of Countries: 019

Patent Family:

CC Number	Kind	Date	Week	
WO 9404181	A1	940303	9410	(Basic)

Priority Data (CC No Date): US 932456 (920817)

Applications (CC,No,Date): WO 93US7653 (930813)

EP and/or WO Cited Patents: 02Jnl.Ref

Designated States

(National): AU; CA; JP

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

Abstract (Basic): WO 9404181 A

A novel peptide capable of neutralising the anticoagulant effects of heparin comprises the sequence (I).

Each Y = Leu, Ile, Val, Phe, Tyr or Trp; each X = Ala, Arg, Asn, Cys, Gln, Gly, His, Ile, Leu, Lys, Met, Phe, Ser, Thr, Trp, Tyr or Val.

USE - The peptides are capable of binding to heparin with sufficient affinity to neutralise its anticoagulant effects. The peptides are used partic. to restore a normal coagulation status in a patient after administration of heparin for e.g. heart surgery, organ transplantation, catheterisation or prevention of blood clot formation.

In an example, peptide RP316, ACLAALKKILKKLLESLGGC-NH<sub>2</sub>, was prepd. by solid phase synthesis on a automated synthesiser using Boc/benzyl protected amino acids and anhydrous HF cleavage/deprotection. RP316 binds heparin with a K<sub>d</sub> of 5.1x10<sup>-7</sup>. In a Factor Xa assay, RP316 was effected as PF4 and protamine at restoring Factor Xa activity inhibited by heparin. In an activated partial thromboplastin time (APTT) assay in normal human plasmin in the presence of heparin, RP316 had 50% of the heparin neutralisation

(cont. next page)

activity of PF4 on a wt./vol. basis. Dwg.0/0  
Derwent Class: B04;  
Int Pat Class: A61K-037/02; C07K-005/10

Record - 4

DIALOG(R)File 351:Derwent WPI  
(c) 1994 Derwent Info Ltd. All rts. reserv.

009685176 WPI Acc No: 93-378730/48  
XRAM Acc No: C93-168101

Rapid inactivation of virus in protein compsn. - by heating briefly,  
with rapid heating and cooling, esp. for treating tissue thromboplastin  
Patent Assignee: (BEHW ) BEHRINGWERKE AG  
Author (Inventor): FREUDENBERG W; KEUPER H; MATZMORR W  
Number of Patents: 005  
Number of Countries: 019  
Patent Family:

CC Number	Kind	Date	Week	
EP 571771	A2	931201	9348	(Basic)
DE 4240103	A1	931202	9349	
AU 9338767	A	931202	9404	
CA 2096888	A	931127	9407	
JP 6065091	A	940308	9414	

Priority Data (CC No Date): DE 4217355 (920526); DE 4240103 (921128)  
Applications (CC,No,Date): JP 93122480 (930525); EP 93106848 (930428); AU  
9338767 (930525); CA 2096888 (930525)

Language: German

EP and/or WO Cited Patents: No-SR.Pub

Designated States

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE

Abstract (Basic): EP 571771 A

Viruses in a prepn. of proteins (placental, plasma or microbially  
produced proteins, or in cell culture) are inactivated by briefly  
heating a soln. of the prepn.. Partic. heating is done indirectly,  
using a heat transfer agent, to 45-95 (esp. 65-80) deg.C. Heating and  
cooling times are less than 30 (esp. 5) sec. with residence time at  
treatment temp. 0.1-20 (esp. 0.5-5) sec..

USE/ADVANTAGE - The method is esp. applied to solns. of  
tissue thromboplastin used (a) as a reagent in rapid screening tests  
for diagnosis of coagulation disorders and (b) therapeutically as a  
'factor 8 by-pass agent' in treatment of haemophilia. This method  
provides complete inactivation more quickly than conventional processes  
(pasteurisation or dry heating) and the heated product suffers no  
significant loss of biological activity. Dwg.0/4

Derwent Class: B04; D16;

Int Pat Class: A61K-037/04; A61K-037/54; A61L-002/04; C07K-001/00;  
C07K-003/00; C12N-001/12; C12N-007/04; C12N-009/48

Record - 5

DIALOG(R)File 351:Derwent WPI  
(c) 1994 Derwent Info Ltd. All rts. reserv.

009675258 WPI Acc No: 93-368811/46  
XRAM Acc No: C93-163747  
XRPX Acc No: N93-284626

(cont. next page)

Test device for rapid and simple blood coagulation assay - comprises membrane impregnated with coagulation initiator and labelled substrate for thrombin, generating signal on activation

Patent Assignee: (AVOC-) AVOCET-MEDICAL INC

Author (Inventor): ZWEIF S E

Number of Patents: 002

Number of Countries: 028

Patent Family:

CC Number	Kind	Date	Week	
WO 9322453	A1	931111	9346	(Basic)
AU 9342875	A	931129	9411	

Priority Data (CC No Date): US 874667 (920427)

Applications (CC,No,Date): AU 9342875 (930414); WO 93US3564 (930414)

Language: English

EP and/or WO Cited Patents: US 3884896; US 4273873; US 4640893; US 4774192; US 4861712

Designated States

(National): AU; BR; CA; FI; HU; JP; KR; NO; NZ; PL; RU; UA

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

Filing Details: AU9342875 Based on WO 9322453

Abstract (Basic): WO 9322453 A

Test device comprises (1) a permeable membrane having opposite application and indicator faces, free of interference with a coagulation pathway; (2) a coagulation initiator (I) impregnated into the membrane and (3) a substrate (II), impregnated in the membrane, which produces a detectable signal when activated by a component (A) of the coagulation pathway. When a whole blood sample is applied to the application face, a detectable signal is produced on the opposed face as a result of prodn. of (A). Pref. the membrane is a hydrophilic, non-swellaable material, specifically polysulphone (PS) with an asymmetric structure which has been treated to inhibit interference with the coagulation pathway.

USE/ADVANTAGE - Device is used to determine the coagulation capacity of a whole blood (finger prick) sample, e.g. in to prothrombin or activated partial thromboplastin tests. Device is simple and reliable enough to be used by patients themselves, requires only a drop of blood (5-30 microl) and reading of the result is automated. Results are not dependent on sample vol. and to membrane is not lytic but does exclude red blood cells from the observation zone.

Dwg.1,2/3

Derwent Class: A96; B04; D16; S03;

Int Pat Class: C12N-011/04; C12N-011/08; C12N-011/14; C12Q-001/56; G01N-021/00; G01N-033/86

Derwent Registry Numbers: 1694-U; 1949-U

## Record - 6

DIALOG(R)File 351:Derwent WPI

(c) 1994 Derwent Info Ltd. All rts. reserv.

009667991 WPI Acc No: 93-361542/46

XRAM Acc No: C93-160235

XRFX Acc No: N93-279116

Determin. of activated partial thromboplastin time - using mixt. of sulphatide(s) and kaolin as coagulation initiator

Patent Assignee: (IMMO) IMMUNO AG

Author (Inventor): LANG H; MORITZ B

Number of Patents: 006

(cont. next page)

Number of Countries: 018

Patent Family:

CC Number	Kind	Date	Week	
EP 570356	A1	931118	9346	(Basic)
NO 9301774	A	931116	9404	
CA 2096212	A	931116	9406	
FI 9302195	A	931116	9406	
JP 6043169	A	940218	9412	
CS 9300879	A2	940216	9414	

Priority Data (CC No Date): AT 92998 (920515); AT 93841 (930430)

Applications (CC,No,Date): CS 93879 (930512); EP 93890099 (930512); NO 931774 (930514); CA 2096212 (930513); FI 932195 (930514); JP 93112783 (930514)

Language: German

EP and/or WO Cited Patents: 3.Jnl.Ref; CH 678892; EP 107383; EP 123883; WO 9116453; WO 9208479

Designated States

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; IE; IT; LI; NL; SE

Abstract (Basic): EP 570356 A

An initiator of the intrinsic coagulation of blood, plasma or their derivs., consists of a mixt. of sulphatides and a solid activator, esp. kaolin. A reagent for determining the partial thrombo-plasma time (a PTT) of blood, plasma or their derivs. clontaing the initiator of the intrinsic coagulation and other phospholipids is also claimed.

USE/ADVANTAGE - The invention facilitates the prepn. of a standardised reagent of high stability in the determination of a PTT, which is simple to handle, economical, has short acitvation time and high sensitivity towards individual factors of the coagulation cascade. The initiator can be lyophilised with phospholipids to give a cheap reagent. Any possible negative reciprocal effect of the individual components is negligible. The resulting reagent can be used in the monitoring of heparin therapy and in the determination of individual factors, that is coagulation factors or inhibitors of intrinsic coagulation. If the reagents is mixed with a heparin neutralising substance, it can be used to determine the aPPT of heparin or heparinoid contg. samples. The presence of sulphatides shortens coagulation time, while the presence of kaolin improves sensitivity.

Dwg.0/0

Derwent Class: B04; S03;

Int Pat Class: A61K-047/02; A61K-047/20; C12Q-001/56; G01N-033/49; G01N-033/86

Derwent Registry Numbers: 0148-U; 1833-U; 1949-U

#### Record - 7

DIALOG(R)File 351:Derwent WPI

(c) 1994 Derwent Info Ltd. All rts. reserv.

009606010 WPI Acc No: 93-299558/38

XRAM Acc No: C93-133231

Protein kinase C inhibitor effective against malignant tumours - contg. (opt. recombinant) calphobindin I

Patent Assignee: (KOWA ) KOWA CO LTD; (KAGA-) ZH KAGAKU OYOBI KESSEN RYOHO KENKYUSHO

Number of Patents: 001

Number of Countries: 001

Patent Family:

(cont. next page)

CC Number	Kind	Date	Week	
JP 5213769	A	930824	9338	(Basic)

Priority Data (CC No Date): JP 9219032 (920204)

Abstract (Basic): JP 05213769 A

Protein kinase C inhibitors contg. as active component calphobindin I (CPB-I) or recombinant CPB-I (r-CPB-I) are new.

CPB-I is extracted from the human or animal organs (Jap. Pat. Kokai no. 62174023) and has the following properties: (1) Mol. wt. 34,000+-2,00 (DSD-polyacrylamide gel electrophoresis; reductive condition); (2) isoelectric point: 4.7 +-0.1 (column electrophoresis using an ampholyte); (3) inactivated by heating at 50 deg.C for 30 min., stable at pH 4-10, stable in plasma at 37 deg.C for 30 min.; (4) prolongs the blood coagulation time in re-addition of Ca, prolongs prothrombin life, and prolongs the active portion life of thromboplastin; (5) constitutive amino acid: aspartic acid, threonine, serine, glutamic acid, proline, glycine, alanine, 1/2 cystine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, histidine, lysine and arginine.

USE/ADVANTAGE - CPB-I strongly inhibits protein kinase C (PKC), whose activity is dependent on Ca<sup>2+</sup> concentration, and is useful in prevention or treatment of malignant tumours caused by abnormal activation of PKC. CPB-I may be applied intravenously at a daily dose of 0.0001-100 mg, partic. 0.001-10 mg, for an adult. Also applicable orally, intramuscularly, percutaneously or rectally.

In an example, to 225 micro liter mixt. of 20 mM tris-HCl (pH 7.4), 10 mM MgCl<sub>2</sub>, 200 micro g/ml histone III-S, 10 microM (gamma-32p) ATP (0.9-1.4 x 10 power 6 cpm), 1 mM CaCl<sub>2</sub> and 20 micro g/ml phosphatidylserine (PS) was added 25 micro liter PKC soln. (0.16 micro g PKC) and incubated at 30 deg.C for 5 min. Then, 2 ml ice-cooled 25% CF<sub>3</sub>COOH (TCA) was added to stop the reaction. Acid-insoluble protein was trapped on a nitrocellulose membrane (Toyo filter; 0.45 micro m in pore size). The filter was washed with 2 ml 25% TCA 5 times, and placed in a scintillation vial contg. 5 ml ACSII (Amersham); the radioactivity of 32p was counted by a liquid scintillation counter (LSC950; Aloka). r-CPB-I was added before addn. of PKC. 50% Inhibition: 0.07 microM CPB-I. Dwg.0/0

Derwent Class: B04;

Int Pat Class: A61K-037/02; A61K-037/64; C07K-013/00

#### Record - 8

DIALOG(R) File 351:Derwent WPI

(c) 1994 Derwent Info Ltd. All rts. reserv.

009442665 WPI Acc No: 93-136182/17

XRAM Acc No: C93-060692

XRPX Acc No: N93-103850

Prepn. of thromboplastin reagent for use in prothrombin time test - by culturing human cells, lysing then isolating and resuspending membrane material

Patent Assignee: (ALKU ) AKZO NV

Author (Inventor): EBERT R F; VALDES-CAMIN R P

Number of Patents: 006

Number of Countries: 022

Patent Family:

CC Number	Kind	Date	Week	
EP 538951	A2	930428	9317	(Basic)
AU 9227176	A	930429	9324	

(cont. next page)



CA 2080428	A	930423	9327
FI 9204774	A	930423	9328
ZA 9207691	A	930728	9335
JP 5276995	A	931026	9347

Priority Data (CC No Date): US 781511 (911022); US 904423 (920626)  
Applications (CC, No, Date): JP 92284462 (921022); EP 92203216 (921020); AU  
9227176 (921020); CA 2080428 (921013); FI 924774 (921021); ZA 927691 (921006)

Language: English

EP and/or WO Cited Patents: No-SR.Pub

Designated States

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT  
; SE

Abstract (Basic): EP 538951 A

Prepn. of a thromboplastin reagent from cultured human cells comprises (a) washing the cells with isotonic aqs. salt soln., (b) lysing the cells in a buffered soln. contg. EDTA and albumin, (c) isolating membranous material from the lysed cells and (d) resuspending the isolated membranous material in an aqs. diluent having a physiologic ionic strength in the range 0.1-0.25.

The diluent pref. comprises 0.5-2.5 wt.% polyethylene glycol, 50-150mM NaCl, 10-50mM Ca-gluconate, 0.01-1wt.% NaN<sub>3</sub>, 0.1-10mg/ml BSA and 5-75 mM imidazole (pH 6.8-7.8).

Also claimed is a thromboplastin reagent prepd. by washing cultured human cells with isotonic aqs. salt soln., physically lysing the cells in a buffered soln. contg. EDTA and albumin, isolating membranous material from the lysed cells and resuspending the isolated membranous material, the reagent having a thromboplastin protein concn., exclusive of added albumin, in the range 0.5-3 mg/ml.

USE/ADVANTAGE - The thromboplastin reagent can be used in a one-step/one-stage prothrombin time (PT) test for determining functional integrity of coagulation factors or for monitoring patients receiving anticoagulant therapy using the reagent, normal human plasma typically clots in 10-14 secs. The reagent is stable in liquid form for at least 8 hrs. at 37degC and 5 days at 4 degC.

Dwg. 1/4

Derwent Class: B04; D16; S03;

Int Pat Class: C07K-015/00; C12N-005/08; C12N-009/64; C12P-021/00;  
C12Q-001/56; G01N-033/531; G01N-033/86

Derwent Registry Numbers: 0195-S; 1151-S; 1193-S; 1327-S; 1706-S; 2044-S;  
2052-S

## Record - 9

DIALOG(R) File 351:Derwent WPI

(c) 1994 Derwent Info Ltd. All rts. reserv.

009260930 WPI Acc No: 92-388343/47

XRAM Acc No: C92-172512

Production of thromboplastin - comprises homogenising brain and muscle tissues of day-old chicken with distilled water, and filtration followed by drying

Patent Assignee: (ANIM=) ANIMALS NONCONTAGIOUS DISEASES RES INST

Author (Inventor): FEDOROVA N M; VOITOV L I

Number of Patents: 001

Number of Countries: 001

Patent Family:

CC Number	Kind	Date	Week
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(cont. next page)

SU 1671305 A1 910823 9247 (Basic)

Priority Data (CC No Date): SU 4616530 (881205)

Abstract (Basic): SU 1671305 A

Brain and muscle tissues obtd. from 24 hours-old chickens are used as the starting biological tissue instead of human brain tissue obtd. from cadavers. The tissue is homogenised with distilled water, and filtered. Drying completes the process. The material is more effective than that extracted from human brain tissues.

USE/ADVANTAGE - Thromboplastin (I) is produced more efficiently. Use of (I) from chickens instead of (I) extracted from human brain tissues reduces the prothrombin time from 39 min. +/- 0.42 sec. to 19 min. +/- 0.28 sec. Bul.31/23.8.91 Dwg.0/0

Derwent Class: B04; D16;

Int Pat Class: A61K-035/12

#### Record - 10

DIALOG(R) File 351:Derwent WPI

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009197559 WPI Acc No: 92-324991/40

XRAM Acc No: C92-144373

High-purity clear thrombin solns. - useful as surgical clotting aids and can be absorbed in haemostatic pads and freeze-dried

Patent Assignee: (WARN ) WARNER LAMBERT CO

Author (Inventor): BOCTOR A; MEHTA S; RADEBAUGH G; BOCTOR A M; MEHTA S C; RADEBAUGH G W

Number of Patents: 006

Number of Countries: 019

Patent Family:

CC Number	Kind	Date	Week	
EP 505604	A1	920930	9240	(Basic)
PT 97311	A	921030	9247	
AU 9173810	A	921015	9249	
CA 2039248	A	920928	9251	
JP 4320683	A	921111	9252	
AU 642987	B	931104	9351	

Priority Data (CC No Date): EP 91105068 (910328)

Applications (CC,No,Date): AU 9173810 (910325); PT 97311 (910410); AU 9173810 (910325); CA 2039248 (910327); JP 91106603 (910412)

Language: English

EP and/or WO Cited Patents: EP 221700; EP 378798; EP 439156

Designated States

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

Filing Details: AU0642987 Previous Publ. AU 9173810

Abstract (Basic): EP 505604 A

Ultra-pure, clear, colourless thrombin solns. are claimed. The solns. have a specific activity of 4000-11,000 units/mg protein.

The solns. are prepd. by (a) reacting prothrombin with purified thromboplastin, pref. in a 10-40 mM CaCl<sub>2</sub> soln. at 10-25 deg.C for 15-45 min.; (b) centrifuging the resulting protein suspension; (c) eluting the supernatant through an anion-exchange agarose column, pref. with 25-50 mM phosphate buffer contg. 0.1 M NaCl; (d) freezing, thawing and centrifuging the eluate; and (e) eluting the supernatant through a cation-exchange agarose column with a 0.1-1 M NaCl gradient in 25 mM phosphate buffer.

USE - The solns. are useful as clotting aids in surgical

(cont. next page)

procedures or may be absorbed in haemostatic pads and freeze-drie  
Dwg.0/0  
Derwent Class: B04; D16;  
Int Pat Class: A61K-037/54; A61K-037/547; C12N-009/74

**Record - 11**

DIALOG(R)File 351:Derwent WPI  
(c) 1994 Derwent Info Ltd. All rts. reserv.

009138158 WPI Acc No: 92-265596/32

XRAM Acc No: C92-118591

New exogenous blood coagulation assay reagent - contains  
(H-D-phenylalanyl-prolyl-arginyl-3-carboxy-4-hydroxy-anilide), tissue  
thromboplastin and calcium salt

Patent Assignee: (NITO ) NITTO BOSEKI CO LTD

Number of Patents: 001

Number of Countries: 001

Patent Family:

CC Number	Kind	Date	Week	
JP 4183400	A	920630	9232	(Basic)

Priority Data (CC No Date): JP 9038669 (901116)

Abstract (Basic): JP 04183400 A

An exogenous blood coagulation assay reagent is claimed and contains a synthetic substrate, tissue thrombo-plastin and Ca salt as principal component. The synthetic substrate is H-D-phenylalanyl-prolyl - arginyl-3-carboxy-4-hydroxy-anilide or its salts, and pref. contain 0.2-15% of polyethylene glycol. Activity of exogenous blood coagulation is assayed by adding a plasma sample to the reagent and incubating, 5-amino-salicylic acid is produced by oxygen reaction of thrombin which is produced by activation with tissue thromboplastin in the reagent. A synthetic substrate in the reagent, is measured, i.e. the oxygen reaction is measured by an end-point method.

USE/ADVANTAGE - Compared with common synthetic substrates, the substrate is barely decomposed with tissue thromboplastin. This is because, the synthetic substrate and tissue thromboplastin can be stored with one another Dwg.0/1

Derwent Class: B04; D16; B03;

Int Pat Class: C12Q-001/56; G01N-033/86

Derwent Registry Numbers: 1895-U; 2044-U

**Record - 12**

DIALOG(R)File 351:Derwent WPI  
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009070561 WPI Acc No: 92-197963/24

XRAM Acc No: C92-090318

XRFX Acc No: N92-149589

Anti-thromboplastin activity of biologically active materials - is determined by coagulation of thrombocyte-free substrate plasma incubated with commercial thromboplastin

Patent Assignee: (KIPH=) KIEV PHARMACOLOGY TOXICOLOGY RES INST

Author (Inventor): KUBRACHENKO S YA; LIPKAN G N; MAKSIMOV YU N

Number of Patents: 001

Number of Countries: 001

Patent Family:

(cont. next page)

CC Number	Kind	Date	Week	
SU 1675767	A1	910907	9224	(Basic)

Priority Data (CC No Date): SU 4666893 (890327)

Abstract (Basic): SU 1675767 A

Antithromboplastic activity of biologically active materials is determined more efficiently by incubating thrombocyte-free substrate plasma with commercial thromboplastin for 4-10 min. at 36.5-37.5 deg.C and determining the time of its coagulation. A mixt. of thromboplastin with test material, without incubation, is used as the control and the time of coagulation is used as the measure of activity.

USE/ADVANTAGE - Used in mdicine, viz. haematology and

clinical pharmacol

the result in a single step, in 30-60 min. Bul.33/7.9.91 Dwg.0/0

Derwent Class: B04; S03;

Int Pat Class: G01N-033/48

### Record - 13

DIALOG(R)File 351:Derwent WPI

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008505873 WPI Acc No: 91-009957/02

XRAM Acc No: C91-004396

XRPX Acc No: N91-007756

Determining functional activity of protein S in human plasma - using activated substrate plasma and bovine thromboplastin and measuring coagulation time

Patent Assignee: (INLI ) INSTRUMENTATION LAB; (INLI ) INSTRUMENTATION LAB SPA; (INLI ) INSTRUMENTATION LAB SRL

Author (Inventor): PREDA L; LOMBARDI A

Number of Patents: 005

Number of Countries: 008

Patent Family:

CC Number	Kind	Date	Week	
EP 406971	A	910109	9102	(Basic)
CA 2019872	A	910108	9113	
JP 3216199	A	910924	9144	
IT 1230744	B	911029	9235	
US 5147805	A	920915	9240	

Priority Data (CC No Date): IT 8921128 (890707)

Applications (CC,No,Date): US 548224 (900629); EP 90201762 (900702); JP 90178478 (900705)

Language: English

EP and/or WO Cited Patents: 3.Jnl.Ref; FR 2571497; WO 8900205

Designated States

(Regional): DE; ES; FR; GB; IT

Abstract (Basic): EP 406971

The activity of protein S in a human plasma sample is determined by combining the plasma sample with activated substrate plasma then combining the mixt. with bovine thromboplastin (bTP) to initiate a coagulation reaction and measuring a parameter related to the time within which the coagulation reaction occurs.

The bTP is pref. provided as an initiating reagent also contg. calcium ions and phospholipids. The activated substrate plasma with which the sample is admixed is pref. formed from a mixt. of plasma deficient in protein S with a protein C activator, e.g. a purified fraction of Agtistodon contortrix venom.

(cont. next page)

USE/ADVANTAGE - The method can be used for determining the functional activity of protein S with greater accuracy, sensitivity and repeatability than previous methods. The determination of protein S is used for diagnosing individuals prone to illnesses of a thrombotic nature. @ (6pp Dwg.No.1/1)@

Abstract (US): 9240 US 5147805 A

Determination of the activity of protein-S in a human plasma sample comprises mixing the sample with activated substrate plasma; then introduction of bovine thromboplastin (contg. phospholipids and Ca(2+) ions; and measurment of the coagulation time.

USE - The process facilitates the diagnosis of thrombotic tendencies.

Dwg. 0/0

Derwent Class: B04; S03; R16;

Int Pat Class: A61B-000/00; C12Q-001/56; G01N-033/68; G01N-033/86

#### Record - 14

DIALOG(R) File 351:Derwent WPI

(c) 1994 Derwent Inf Ltd. All rts. reserv.

008306403 WPI Acc No: 90-193404/25

XRAM Acc No: C90-083688

Extn. of thromboplastin from tissue with nonionic detergent soln. - or chaotropic agent, and opt. barium sulphate and salt, giving improved sensitivity for measuring prothrombin time

Patent Assignee: (BAXT ) BAXTER INT INC; (BAXT ) BAXTER DIAGNOSTICS INC

Author (Inventor): HAWKINS P L H; MAYNARD J R

Number of Patents: 009

Number of Countries: 016

Patent Family:

CC Number	Kind	Date	Week	
WO 9005740	A	900531	9025	(Basic)
CA 2002208	A	900523	9031	
DK 9001730	A	900719	9046	
EP 396733	A	901114	9046	
NO 9003261	A	900720	9046	
JP 3503534	W	910808	9138	
US 5270451	A	931214	9350	
EP 396733	B1	940105	9402	
DE 68912115	E	940217	9408	

Priority Data (CC No Date): US 276083 (881123)

Applications (CC,No,Date): DE 612115 (891103); WO 89US4867 (891103); EP 90900532 (891103); EP 90900532 (891103); JP 89500744 (891103); US 926134 (920806); WO 89US4867 (891103); EP 90900532 (891103)

Language: English

EP and/or WO Cited Patents: US 3522148

Designated States

(National): DK; JP; NO

(Regional): AT; BE; CH; DE; FR; GB; IT; LU; NL; SE; LI

Filing Details: DE68912115 Based on EP 396733; DE68912115 Based on WO 9005740; EP0396733 Based on WO 9005740

Abstract (Basic): WO 9005740 A

Extn. of thromboplastins (I) comprises (1) contacting appropriate tissue with an extractant contg. BaSO<sub>4</sub>, nonionic detergent (II), chaotropic ions (III) and salt, then (2) sepg. extracted (I) from the depleted tissue and BaSO<sub>4</sub>.

Or extractant contains only (III); (III) plus salt; BaSO<sub>4</sub>, (II)

(cont. next page)

and salt, or (III), BaSO<sub>4</sub> and salt.

Also new are extracted (I) compsns. with approx. normal prothrombin time (PT) and increased sensitivity to factor deficiencies and coumadin therapy. Pref. the extractant is about 100 ml per 5g tissue (esp. rabbit brain powder), and treatment is at 43-47 deg.C. for about 15 mins..

USE/ADVANTAGE - (I) are used to measure PT, i.e. as screening reagents for blood coagulation factor deficiencies and for monitoring oral anti-coagulant therapy using coumadin. They provide improving sensitivity for all PT-based tests and assays; are more stable when reconstituted than Thromboplastin FS; require less extract and are optically less dense. @ (25pp Dwg.No.0/0)

Abstract (US): 9350 US 5270451 A

Method comprises (a) contacting tissue contg. thromboplastin with an extn. fluid comprising 0.1-1.0 g BaSO<sub>4</sub> per g tissue, 0.01-0.25% a nonionic detergent, 5-100 mM chaotropic ion, and a salt; and (b) sepg. the extracted thromboplastin from depleted tissue and BaSO<sub>4</sub>.

Amt. of extn. fluid is pref. 100ml per 5g tissue. Salt concn. is 30-180 mM. Extn. temp. is 43-47 deg. C for 15 mins. Tissue is rabbit brain powder.

USE/ADVANTAGE - Used in screening tests for blood coagulation deficiencies and for monitoring oral anti-coagulant therapy using coumadin. Extn. of thromboplastin reagents enhances sensitivity. Dwg.0/0

Abstract (EP): 9402 EP 396733 B

A method for extracting thromboplastins comprising: (a) contacting tissue containing thromboplastin with an effective amount of extraction fluid under conditions which result in the extraction of thromboplastin, and (b) separating said extracted thromboplastin from said depleted tissue characterised in that the extraction fluid comprises:- i) chaotropic ions, or ii) nonionic detergent, barium sulphate and a salt. Dwg.0/0

Derwent Class: B04;

Int Pat Class: A61K-037/02; C07K-003/02; C07K-003/24; C07K-003/74;

C07K-013/00; C07K-015/06; C12N-009/10

Derwent Registry Numbers: 1739-U

## Record - 15

DIALOG(R)File 351:Derwent WPI

(c) 1994 Derwent Info Ltd. All rts. reserv.

007949323 WPI Acc No: 89-214435/30

XRAM Acc No: C89-095339

Concentrates of coagulation factors II, VII, IX and/or X - obtd. from plasma, etc., by chromatography on diethylamino-ethyl-poly-hydroxyethyl (meth)acrylate; METHACRYLATE

Patent Assignee: (RYBA/) RYBAK M; (TESS-) TESSEK SDRUZENI PRA; (TESS-) TESSEK SDRUZENI

Author (Inventor): HOUSKOVA J; KASAFIREK E; LOSTICKY C; SEDLMAIER O; ULRYCH S; KASAFIREK F; ROUBALOVA A; RYBAK M

Number of Patents: 006

Number of Countries: 010

Patent Family:

CC Number	Kind	Date	Week	
EP 325225	A	890726	8930	(Basic)
CS 8800324	A	890712	8937	
DK 8900217	A	890719	8939	
CS 8802890	A	890814	8942	

(cont. next page)

JP 1294697 A 891128 9002  
US 5118614 A 920602 9225

Priority Data (CC No Date): CS 88324 (880118); CS 88869 (880212); CS 882890 (880428)

Applications (CC,No,Date): US 297753 (890117); EP 89100788 (890118); JP 897888 (890118)

Language: English

EP and/or WO Cited Patents: 1.Jnl.Ref; A3...9018; EP 208215; EP 229234; EP 303329; No-SR.Pub; US 4637932

Designated States

(Regional): CH; DE; FR; GB; IT; LI

Filing Details: EP0325225 (12.2.88-CS-000869) (1762TF)

Abstract (Basic): EP 325225

Concentrates of blood coagulation factors II, VII, IX and/or X are new, obtainable by contacting a biological material contg. the factors with a sorbent based on DEAE-poly(hydroxyethyl acrylate) and/or DEAE-poly(hydroxyethyl methacrylate) i.e. DEAE-HE(M)A, and desorption with a buffer soln. of pH 7.2-7.6 with saline concn. 0.3-.0M.

Also claimed ar

quantitative determination of factor VII in biological materials, using concentrates of factors II and X, pref. prepd. as above.

USE - Useful in treatment of hereditary and acquired clotting defects, damage to the liver parenchyma, vitamin K deficiency, acute haemorrhage, etc., or for pre-surgery prophylaxis of bleeding, and in diagnosis of coagulation disorders, etc. Factors II and X are used in detection or determination of factor VII in body fluids, partic. plasma, plasma fractions or urine, milk, milk prods., etc., as an indicator of inflammatory disease, e.g. urogenital diseases or mastitis in cattle. The DEAE-HE(M)A sorbents are resistant to microbial contamination and maintain their qualities on changing physical or chemical conditions (c.f. DEAE-polysaccharides previously used). @ (12pp Dwg.No.0/0)@

Abstract (US): 9225 US 5118614 A

Blood coagulation factor concentrate comprises coagulation factors II, VII, IX and X.

Prepn. of this concentrate comprises adsorption of the factors from human and/or animal blood plasma, or their active fractions, using an adsorbent based on (co)polymers of diethylaminoethyl-hydroxyethyl (meth)acrylates or their mixts; then selective elution with aq. NaCl solns. (0.3-2.0 mol dm<sup>-3</sup>) at pH 7.2-7.6.

USE - Factor II and X concentrates and thromboplastin, phospholipids, Ca(2+) ions and a chromogenic substrate give a marked colour change when mixed with body fluid samples contg. factor VII, and the intensity of colour is a measure of the amt. of factor VII present and the extent of inflammatory disease.

Derwent Class: A96; B04; C03;

Int Pat Class: C07K-003/20; C12N-009/64; C12Q-001/56; C07K-015/06; G01N-033/50; G01N-021/78

Derwent Registry Numbers: 1895-U

#### Record - 16

DIALOG(R) File 351:Derwent WPI

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007523260 WPI Acc No: 88-157193/23

XRAM Acc No: C88-070056

(cont. next page)

Anticoagulant derived from human placenta - by removing amnion, washing with physiological saline, homogenising centrifuging and extracting active substrate with chelating agent

Patent Assignee: (KOWA ) KOWA KK

Number of Patents: 001

Patent Family:

CC Number	Kind	Date	Week
JP 63096131	A	880427	8823 (Basic)

Priority Data (CC No Date): JP 86243777 (861014)

Abstract (Basic): JP 63096131

Anti-coagulant derived from human placenta has: (1) mol.wt. (by SDS-PAGE, reduced condition and no-reduced condition): 33,000+/-2,999; (2) isoelectric point (ampholite electrophoresis): 6.2+/-0.1; (3) stability ; inactivated after treatment at 50 deg.C for 30 min., stable at pH 4-8.5 (37 deg.C) and stable at 37 deg.C for 30 min. in plasma;

(4) action ; p

prothrombin time and prolongs activated partial thromboplastin time.

Prepn. involves removing amnion, washing human placenta with physiological saline and homogenising. Obtd. homogenate is centrifuged and active substance is extracted and purified from the ppt. using chelating agents such as EDTA, EGTA, oxalic acid, citric acid, etc.. Detergents such as triton X-100, SDS and deoxycholic acid can be used for the extraction. The extract is subjected to pptn. with 35-85% satd. (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, dialysis, ion-exchange chromatography and gel filtration.

The anti-coagulant is administered as an injection. Pref. dose is 10 microg-10 mg/kg-day. When making a preparation, a stabiliser such as albumin, gelatin and mannitol is added.

USE/ADVANTAGE - The anti-coagulant exhibits strong anti-coagulant activity, esp. when tissue thromboplastin activity is high. The anti-coagulant is safe and has no side effects. @(11pp Dwg.No.0/0)@

Derwent Class: B04;

Int Pat Class: A61K-035/50; C07K-003/02; C07K-015/06

#### Record - 17

DIALOG(R)File 351:Derwent WPI

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007109637 WPI Acc No: 87-109634/16

XRAM Acc No: C87-045569

XRPX Acc No: N87-082490

Photometric assay of protein C, esp. in plasma by sequential incubation with thrombin, excess thrombin inactivator and then chromogenic thrombin substrate

Patent Assignee: (BOEF ) BOEHRINGER MANNHEIM GMBH

Author (Inventor): BARTL K; DESSAUER A; LILL H

Number of Patents: 005

Patent Family:

CC Number	Kind	Date	Week
DE 3536903	A	870416	8716 (Basic)
JP 62093665	A	870430	8723
AU 8664126	A	870514	8726
EP 229234	A	870722	8729
DD 250187	A	870930	8808

Priority Data (CC No Date): DE 3536903 (851016)

Applications (CC,No,Date): JP 86244328 (861016); EP 86114361 (861016)

Language: German

EP and/or WO Cited Patents: US 4214049; EP 182929; 6.Jnl.REF

Designated States

(cont. next page)



(Regional): AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE  
Abstract (Basic): DE 3536903

Photometric determin. of protein C (I) comprises first incubating the sample with thrombin (II) to form activated (I). Then excess of thrombin inhibitor is added and the decrease of (II) formation from prothrombin (III) (mediated by the coagulation factors) determined using a chromogenic thrombin substrate (IV).

Pref. the thrombin inhibitor is antithrombin III (AT), opt. used together with heparin, and pref. (IV) are H-D-Phe-Pip-Arg-pNA or Tus-Gly-Pro-Arg-pNA (pNA =p-nitroaniline).

Pref. the assay is carried out in pH 6-9 buffer, opt. in presence of usual stabilisers and preservatives. AT is generally added at 1-200 mlof test sample, with an excess of over 20% relative to the (II)

activity. Since

factors V and VIII, the coagulation system is modified by adding coagulation activators, or the factors themselves. Esp. a factor XII activator (particularly ellagic acid plus cephalin); or a factor VII activator (particularly thromboplastin) plus factor V; or factor Xa (an activator for factor II) plus cephalin can be added.

USE/ADVANTAGE - Assay of (I) is useful in diagnosis of e.g. liver disease; coagulopathy; inherited venous thrombo-embolism; thrombosis; etc.. This method is simple and, unlike the known method, does not require enzyme-labelled antibodies. @(10pp Dwg.No.0/4)@

Derwent Class: B04; S03; R16;

Int Pat Class: G01N-033/68; C12Q-001/34; G01N-021/75

#### Record - 18

DIALOG(R)File 351:Derwent WPI

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007057978 WPI Acc No: 87-057975/09

Related WPI Accession(s): 92-143152; 92-161105; 93-265863

XRAM Acc No: C87-024124

XRPX Acc No: N87-043933

Analyte determin. in a fluid - using a device having a capillary unit acting as the motive force for moving the fluid

Patent Assignee: (BIOT-) BIOTRACK INC; (BIOT-) BIOTRACK

Author (Inventor): COBB M E; HILLMAN R S; OSTOICH V E; WINFREY L J; ALLEN J D; GIBBONS I

Number of Patents: 016

Number of Countries: 017

Patent Family:

CC Number	Kind	Date	Week	
EP 212314	A	870304	8709	(Basic)
AU 8660884	A	870212	8715	
JP 62129759	A	870612	8729	
US 4756884	A	880712	8830	
US 4948961	A	900814	9035	
US 4963498	A	901016	9044	
CA 1275231	C	901016	9047	
US 5004923	A	910402	9116	
US 5140161	A	920818	9236	
US 5144139	A	920901	9238	
US 5164598	A	921117	9249	
US 5300779	A	940405	9413	
EP 212314	B1	940427	9417	
JP 6094722	A	940408	9419	
JP 6094723	A	940408	9419	

(cont. next page)

JP 6094724 A 940408 9419

Priority Data (CC No Date): US 762748 (850805); US 880793 (860701)  
Applications (CC,No,Date): JP 86182050 (860804); JP 92219280 (860804); EP  
86110184 (860724); JP 86182050 (860804); US 177625 (880405); US 144416  
(880115); US 472130 (900130); US 880793 (860701); US 177625 (880405);  
US 472130 (900130); US 651283 (910205); US 734597 (910723); US 762748 (  
850805); US 880793 (860701); US 177625 (880405); US 472130 (900130); US  
651283 (910205); US 732596 (910719); US 762748 (850805); US 880793 (  
860701); US 177625 (880405); US 472130 (900130); US 651283 (910205); US  
762748 (850805); US 880793 (860701); US 177625 (880405); US 472130 (  
900130); US 651283 (910205); US 931719 (920818); EP 86110184 (860724);  
JP 86182050 (860804); JP 92219281 (860804); JP 8612050 (860804); JP

92219282 (8608

Language: English

EP and/or WO Cited Patents: 3.Jnl.Ref; A3...8929; AT 376300; DE 2007405; DE  
3134611; No-SR.Pub; US 3799742; US 4088448; US 4233029; 2.Jnl.Ref

Designated States

(Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE

Filing Details: US5140161 Div ex US 4756884; US5140161 Div ex US  
4948961; US5144139 Div ex US 4756884; US5144139 Div ex US 4948961  
; US5144139 Cont of US 5004923; US5164598 Div ex US 4756884;  
US5164598 Div ex US 4948961; US5164598 Cont of US 5004923;  
US5300779 Div ex US 4756884; US5300779 Div ex US 4948961;  
US5300779 Cont of US 5004923; US5300779 Cont of US 5164598

Abstract (Basic): EP 212314 A

A method for determining an analyte in a fluid medium uses a device comprising at least one capillary unit acting as the motive force for moving the fluid medium in the device, at least one chamber unit, an inlet port, an outlet port distant from the inlet port and a reagent contained within the device, the reagent being a member of a detection system, where the capillary acts as a metering pump and flow controller of the assay medium through the device to provide for a time controlled reaction with the reagent.

A fluid sample is introduced through the inlet port into one of the units, and the fluid allowed to transit from one unit to the next unit at a rate controlled by the capillary unit and react with the reagent resulting in a detectable signal produced by the detection system. Pref. the device is made from acrylonitrile-butadiene-styrene copolymer.

USE/ADVANTAGE - The method can be used with a wide variety of fluids, partic. physiological fluids, for detection of e.g. drugs, pathogens, glucose or serum enzymes. The devices provide for simple measurements of volumes, mixing of reagents, incubations and visual or instrumental determ. of the result. Dwg.0/8

Abstract (US): 9413 US 5300779 A

An assay based on measuring blood coagulation time is performed by inserting into an electronic monitor a housing with a capillary passage (12) between an inlet port (14) and a vent (22), and reagent (16) inducing blood clotting on the passage surface, and introducing a sample into the port before or after placing in the monitor.

The monitor detects coagulation by sensing interaction of light with particles in the passage, and the measured coagulation time is related to the presence or amount of analyte. In partic., the reagent is thromboplastin, and the sample is whole blood or blood from which red cells have been removed. The housing is e.g. of injection-moulded ABS.

ADVANTAGE - Allows individual assays to be carried out rapidly and accurately with min. equipment.

Dwg.1/8 9249 US 5164598 A

(cont. next page)

A system for detecting the presence of an analyte in or a characteristic of blood comprises a housing (50) with a capillary passage (76) for drawing in blood solely by capillary attraction, and a reagent in the passage causing the blood to clot. A monitor can hold the housing and pass light through the passage to detect and analyse light scattering to determine when clotting occurs.

The housing is pref. hydrophobic and has at least a part of the walls treated to be hydrophilic, the passage having hydrophilic walls. The reagent is a member of a system providing a detectable signal in relation to the analyte or characteristic. The housing is pref. fored of cellulose acetate, polystyrene or ABS.

USE/ADVANTAGE - E.g

crosslinked fibrin dimer, or direct or indirect blood grouping, permits rapid and convenient testing.

Dwg.2A/8 9238 US 5144139 A

Agglutination of particles is detected by adding a fluid sample to a capillary passageway in a cartridge contg. a diagnostic reagent that reacts with the sample to produce an agglutination system, and passing a light beam (e.g. laser) through the sample to detect agglutinated particles.

ADVANTAGE - Rapid testing.

Dwg.2a/8 9236 US 5140161 A

An analyte in a blood sample is determined using a device with a capillary passageway (76) for moving blood into the device and which contains a reagent interacting with the blood to cause a change in fluidity to provide a detectable signal. Change in fluidity is used as a measure of the presence of an analyte or a property of the sample.

The detectable signal is pref. change in sample flow rate, clotting of the sample or a change in light transmission or emission. The device may be made as an injection moulding of e.g. ABS, and the reaction may involve the binding of members of a pair or an enzyme reaction.

ADVANTAGE - Permits rapid determination with min. user manipulation.

Dwg.2a/8 9116 US 5004923

Control device for detecting depletion of a particle contg fluid from a sample reservoir comprises (a) a light source to impinge on fluid in the reservoir, (b) and a light detector close to a capillary exiting the reservoir to collect light reflected by the particles. (c) A signal generator attached to the light source and (d) a filter operably attached to the output of the detector.

ADVANTAGE - Easier analysis of red cell blood count. @(20pp)@ 9044 US 4963498

Analytical flow process comprises monitoring the flow of test sample soln. and reagent(s) through a narrow tube under the combined effects of capillary force and gravitation by measurement of colour intensity, optical refraction, viscosity, conductance, etc; and comparison of the results with those obtd. using standard solns.

USE - The process is an aid for rapid clinical analysis and diagnosis. @(20pp)@ 9035 US 4948961

A control device capable of simulating the flow of a particle-contg. fluid that is being measured by an analytical instrument utilising an analysis cartridge with an internal chamber through which particulate contg. fluids pass is provided. The device comprises a control cartridge, a liq. crystal cell within said cartridge such to interpose between a light source and a light detector in the analytical instrument. A polarizing filter is provided close to the liq. crystal cell in the control cartridge so as to alternately allow and block passage of light between the light source and the detector when the voltage applied to the cell is modulated.

(cont. next page)

USE - For rapid analytical testing. @(20pp)@ 8830 US 4756884  
Analytical device for detecting the presence of an analyte in a physiological fluid comprises a first capillary unit for pumping a liquid from an inlet part to a chamber in a housing, and a second capillary unit between the chamber and an exit.

The housing contains a reagent of cpds. affecting blood clotting and antibodies. Two chambers may be disposed in the capillary path.

ADVANTAGE - Automatic monitoring of medicines. @(20pp)@

Abstract (EP): 9417 EP 212314 B

A method for determining the presence of an amount of an analyte in, or a property of, a fluid sample comprising: applying said sample to a device (10) comprising an entry port (14) for said sample, a vent (22), a capillary pathway containing a chamber (12,20) connecting said entry port (14) to said vent (22), and a reagent (16,24) in said capillary pathway (12,20), wherein said sample flows through said capillary pathway (12,20) under capillary forces and interaction of said reagent (16,24) with said sample modifies viscosity of said sample or a characteristic of said sample associated with said flow; allowing said sample to interact with said reagent (16,24) and traverse at least a portion of said capillary pathway (12,20); detecting said viscosity or flow characteristic; and relating said viscosity or flow characteristic to the presence or amount of said analyte in or, to said property of, said fluid sample.

Dwg.1/8

Derwent Class: A89; B04; D15; J04; S03; S05;

Int Pat Class: B01L-003/00; B29C-065/08; G01D-018/00; G01N-011/04;  
G01N-021/03; G01N-021/49; G01N-021/51; G01N-031/22; G01N-033/48;  
G01N-033/50

#### Record - 19

DIALOG(R)File 351:Derwent WPI

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004710188 WPI Acc No: 86-213530/33

XRAM Acc No: C86-091847

Photometric determ. of pro-kallikrein in plasma by incubating with surface activator and then with chromogenic thrombin substrate

Patent Assignee: (BOEF ) BOEHRINGER MANNHEIM GMBH

Author (Inventor): BARTL K; LILL H

Number of Patents: 010

Patent Family:

CC Number	Kind	Date	Week	
EP 190766	A	860813	8633	(Basic)
DE 3504405	A	860814	8634	
JP 61185199	A	860818	8639	
NO 8600200	A	860901	8642	
DK 8600621	A	860809	8645	
ES 8701842	A	870301	8715	
US 4732860	A	880322	8815	
EP 190766	B	890531	8922	
DE 3663684	G	890706	8928	
CA 1267598	A	900410	9019	

Priority Data (CC No Date): DE 3504405 (850208)

Applications (CC,No,Date): EP 86101608 (860207); ES 551764 (860207); US 822364 (860124)

Language: German

EP and/or WO Cited Patents: A3...8650; US 4016042; 7.Jnl.REF

Designated States

(cont. next page)

(Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE  
Abstract (Basic): EP 190766

Photometric determination of prokallikrein (I) in plasma comprises incubating the sample with a surface activator (A), measuring the extinction, then adding a chromogenic thrombin substrate (II). The optically-determinable gp. released is measured at short time intervals (or continuously) and the gradient of the linear part of the extinction/time plot used as a measure of (I) content. Pref. Ca ions are added to the test soln., esp. at 1-100 micromoles/ml.

USE/ADVANTAGE - Measurement of (I) is used to assess the status of the blood coagulation system. This method is simple and rapid, and can be carried out at room temp. @(14pp Dwg.No.0/3)@

Abstract (US): 8815 US 4732860

Simultaneous photometric determination of prekallikrein in a

plasma sample and comprises (a) incubating sample with a surface activator along with Ca-ions and a phospholipid to form a reaction mixt.; (b) measuring its extinctions; (c) adding a chromogenic substrate specific to thrombin to the mixt.; and (d) measuring an optically-determinable gp. liberated from the substrate by measuring its extinction at short intervals or continuously.

Incubation takes place at 20-40 deg. C, and a gradient of a linear part of a curve obt'd. by plotting time against extinction of the mixt. simultaneously determined as a measure of prekallikrein content and partial thromboplastin time by measuring the time it takes extinction to reach a predetermined level.

ADVANTAGE - Incubation does not need to be at 0 deg. C enabling automation of the process. @(7pp)@

Abstract (EP): 8922 EP 190766

Process for the simultaneous photometric determination of prokallikrein and of the partial thromboplastin time (PTT) in plasma, characterised in that one incubates plasma with a surface activator of the group ellagic acid, sulphatides and finely-divided silicon dioxide, then adds thereto a chromogenic thrombin substrate, measures the extinction obtained and thereafter measures the optically determinable group liberated therefrom at short time intervals or continuously and determines the gradient of the linear part of the curve obtained by plotting the time against the extinction as measured of the prokallikrein content and the time up to the achievement of a predetermined extinction as PTT. @(8pp)@

Derwent Class: B04; J04; R16

Int Pat Class: C12Q-001/38; G01N-033/86; C12Q-000/00; G01N-021/78

Derwent Registry Numbers: 1694-U

## Record - 20

DIALOG(R) File 351:Derwent WPI

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004430825 WPI Acc No: 85-257703/42

XRAM Acc No: C85-111529

XRPX Acc No: N85-192633

Reagent for photometric measurement of thromboplastin time contg.

thromboplastin and chromogenic substrate which is only slowly cleaved

Patent Assignee: (BEHW ) BEHRINGWERKE AG

Author (Inventor): KOLDE H J

Number of Patents: 010

Patent Family:

CC Number	Kind	Date	Week
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(cont. next page)

EP 158254	A	851016	8542	(Basic)
DE 3413311	A	851017	8543	
AU 8540892	A	851017	8547	
JP 60230066	A	851115	8601	
DK 8501549	A	851010	8603	
ES 8700323	A	870101	8710	
EP 158254	B	880608	8823	
DE 3563222	G	880714	8829	
US 4784944	A	881115	8848	
CA 1258221	A	890808	8938	

Priority Data (CC No Date): DE 3413311 (840409)

Applications (CC,No,Date): EP 85103896 (850401); JP 8572846 (850408); ES 542020 (850408); US 720348 (850405)

Language: German

EP and/or WO Cited Patents: EP 14039; EP 62310; DE 3113350; GB 917012; US 4169015; EP 3474

Designated States

(Regional): AT; BE; CH; DE; FR; GB; IT; LI; L; NL; SE

Abstract (Basic): EP 158254

Reagent for photometric determination of the thromboplastin time contains at least one proteolytically active thromboplastin (TP) and a chromogenic substrate (I) for thrombin. The new feature is that (I) is converted by TP in aq. suspension in presence of Ca ions to below 0.00125 times the initial concn. per hr at 37 deg.C. Pref. the reagent contains (1) 0.5-10 (esp.5) mM Ca ions; (2) 0.005-0.1 (esp. 0.025) M buffer for pH 7-8.5 (esp. 7.6); (3) 0.01-0.2 (esp. 0.05) M neutral salt (esp. NaCl); (4) 0.01-0.5 (esp. 0.25) mg/l 'Polybren' (RTM).

USE - The reagent is used for determination of the blood clotting factors II, VII, X and V. @ (14pp Dwg.No.0/1)@

Abstract (US): 8848 US 4784944

Reagent for photometric determination of prothrombin time comprises a freeze-dried mixt. of thromboplastin having proteolytic activity, hexadimethrine bromide and an ANBA chromogenic substrate for thrombin. The substrate is one converted by the thromboplastin in aq. suspn. in presence of Ca ions, to the extent of less than 0.00125 times its initial concn. per hr. at 37 deg.C.

The thromboplastin is obtainable from human plasma, a Ca ion source, human or animal factor V, buffer or salt may also be present.

USE/ADVANTAGE - In monitoring oral antioagulant therapy, a sensitive response is obtd. @ (4pp)@

Abstract (EP): 8823 EP 158254

A reagent for the photometric determination of the prothrombin time, containing, at the least, a thromboplastin having proteolytic activity and a chromogenic substrate for thrombin of the structure H-D-Phe-Pro-Arg-ANBA-R or Tos-Gly-Pro-Arg-ANBA-R, where R is NH-CnH<sub>2n+1</sub>(sic), with n = 1 to 7, NH-benzyl or the residue of an amino acid, or its alkyl ester, which are bonded via the alpha-amino group, and where the substrate is converted by the thromboplastin, in aqueous suspension in the presence of calcium ions, to the extent of less than 0.00125 times the initial concentration per hour at 37 deg. C. @ (7pp)@

Derwent Class: B04; J04; S03; R16

Int Pat Class: C12Q-001/56; G01N-033/86; A61K-035/16; C12Q-000/56

Derwent Registry Numbers: 1895-U

## Record - 21

DIALOG(R) File 351:Derwent WPI

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(cont. next page)

004270389 WPI Acc No: 85-097267/16

XRAM Acc No: C85-042378

XRPX Acc No: N85-072747

Determn. of blood plasma thromboplastin activity in which coagulation times of thrombocyte-free donor and test plasma are determined and thrombocyte activity is calculated by formula

Patent Assignee: (TYUM=) TYUMEN MEDIC INST

Author (Inventor): BYSHEVSKII A S H; TERSENOV O A; USOLTSEVA V A

Number of Patents: 001

Patent Family:

CC Number	Kind	Date	Week
SU 1114951	A	840923	8516 (Basic)

Priority Data (CC No Date): SU 3615465 (830705)

Abstract (Basic): SU 1114951

Samples of a plasma, free of thrombocytes, taken from 5-6 donors, are mixed and then spun in a centrifuge for 60 mins. to remove any fragments of cell membrane and to obtain a substrate plasma without thromboplastin. The coagulation times of mixts. of various volumes of the donated thrombocyte-free and substrate thromboplastin-free plasma are then determined.

The coagulation times of various volumes of the test blood, free of platelets and substrate plasma, are then determined and the activity of thromoplastin in the test blood is calculated by formula:  $A = (t_1/t_2) \cdot 100$ , where  $t_1$  is the coagulation time of the donor plasma and  $t_2$  is the coagulation time of the investigated plasma. The method allows an accurate determn. of the specific activity of thrombocytes, by studying the effect of a test plasma on the coagulation time of substrate plasma, the thrombocyte content of which has been reduced in a centrifuge.

USE - Determn. of the activity of the coagulating factors of blood in clinic-diagnostic laboratories. Bul.35/23.9.84. @(3pp Dwg.No.0/0)@

Derwent Class: B04; S03; R16;

Int Pat Class: G01N-033/48

## Record - 22

DIALOG(R) File 351:Derwent WPI

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004105617 WPI Acc No: 84-251158/41

XRAM Acc No: C84-105982

XRPX Acc No: N84-187529

Determn. of activated partial thromboplastin time using reagent contg. phospholipid, calcium, chromogenic substrate and sulphatide activator

Patent Assignee: (BEHW ) BEHRINGWERKE AG

Author (Inventor): KOLDE H J

Number of Patents: 013

Patent Family:

CC Number	Kind	Date	Week
DE 3311287	A	841004	8441 (Basic)
EP 123883	A	841107	8445
AU 8426211	A	841004	8447
NO 8401231	A	841022	8449
JP 59187800	A	841024	8449
DK 8401090	A	840929	8501
ZA 8402240	A	840919	8502
ES 8505115	A	850716	8551
CA 1250213	A	890221	8913

(cont. next page)

IL 71370 A 890630 8931  
EP 123883 B 910918 9138  
DE 3485067 G 911024 9144  
JP 91065958 B 911015 9145

Priority Data (CC No Date): DE 3311287 (830328)

Applications (CC,No,Date): EP 84101163 (840322); JP 8457507 (840327); ZA 842240 (840327); EP 84103163 (840322)

Language: German

EP and/or WO Cited Patents: A3...8806; US 3486981; EP 34122; EP 20895; 9.Jnl.REF; 6.Jnl.REF

Designated States

(Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE

Abstract (Basic): DE 3311287

Reagent for this process, opt. in lyophilised form and opt. a lso contains a buffer (esp. HEPES, pH 7.2-8.5), an amino acid and serum albumin.

The substrates are pref. of frmula (I). In (I) R = 1-5C alkyl or

-CH.CH(CH3)

are commercially available; pref. prods. have Rf values 0.25 and 0.31 when subjected to silica gel t.l.c. using, respectively, 65:25:4 chloroform-methanol-water and 40:15 chloroform-methanol as mobile phases. They are used at 0.1-50 microg/ml. The phospholipid is pref. derived from human thrombocytes or placental extract.

USE/ADVANTAGE - Determination of APTT provides information of the status of the endogenous blood coagulation system and is useful in control of heparin therapy. Method requies only a single reagent, which can be freeze-dried to a stable prod. when serum albumin (0.1-1%) is included. The amino acid improves the heparin sensitivity and the reaction can be applied to coagulation-deficient samples. @(12pp Dwg.No.0/0)@

Abstract (EP): 9138 EP 123883

A method for the determination of the activated partial thromboplastin time (APTT) by means of a chromogenic substrate and activation by sulfatides or mixtures of sulfatides, wherein all the reagents, apart from the sample, necessary for carrying out the test are added in one step. @(8pp)@

Derwent Class: B04; S03; R16;

Int Pat Class: G01N-033/86; C12Q-001/56; G01N-000/00

Derwent Registry Numbers: 1895-U

## Record - 23

DIALOG(R) File 351:Derwent WPI

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003901583 WPI Acc No: 84-047127/08

XRAM Acc No: C84-020072

XRPX Acc No: N84-035624

Factor X quantitative analysis in blood plasma by mixing substrate plasma with dil. plasma, coagulation and determin. of prothrombin time

Patent Assignee: (TYUM=) TYUMEN MEDICINE INS

Author (Inventor): BYSHEVSKII A S H; TERSENOV O A; STASENKO S Y A

Number of Patents: 001

Patent Family:

CC Number	Kind	Date	Week
SU 1010562	A	830407	8408 (Basic)

Priority Data (CC No Date): SU 3331993 (810805)

Abstract (Basic): The proposed method involves: obtaining the substrate plasma by adding (to mixed citrate human plasma) a weakly-basic anion

(cont. next page)



exchanging dextran gel (contg. diethyl aminoethyl functional gps. with preference for ionic exchange with proteins of mol. wt. 30-200 thousand dalton at ionic strength 0.25M); pptg. the gel by settling; then sepg. off the supernatant substrate plasma; using a thromboplastin-calcium mixt. as the coagulation activator. As previously, the quantitative analysis of factor X in blood plasma involves: prepn. of a substrate plasma; mixing it with normal dil. plasma; adding a coagulating activator to the mixt. determining the prothrombic time of the mixt.

Typically, the proposed method reduced the coagulation time from 168 to 125 secs. On freezing substrate plasma, the coagulation time (in presence of factor X and thromboplastin-Ca mixt.) was reduced from 26-235 to 134-143 secs. This indicated high preservation of native

properties in t

fold per test. Bul. 13/7.4.83. (3pp Dwg. No. 0/0)

Derwent Class: B04; S03; R16;

Int Pat Class: G01N-033/48

#### Record - 24

DIALOG(R) File 351:Derwent WPI  
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003704371 WPI Acc No: 83-700550/27

XRAM Acc No: C83-062084

XRPX Acc No: N83-115111

Factor VII-sensitive thromboplastin prodn. by extn. of mammalian tissue acetone dry powder with salt soln. contg. calcium ions

Patent Assignee: (BOEF ) BOEHRINGER MANNHEIM GMBH

Author (Inventor): BECKER U; SCHAICH E; WEIGERT M

Number of Patents: 013

Patent Family:

CC Number	Kind	Date	Week	
DE 3150596	A	830630	8327	(Basic)
EP 83773	A	830720	8330	
NO 8204279	A	830718	8335	
DK 8205400	A	830822	8340	
JP 58154515	A	830914	8343	
US 4416812	A	831122	8349	
ZA 8209315	A	830822	8402	
DD 208811	A	840411	8432	
ES 8402942	A	840516	8426	
EP 83773	B	850522	8521	
DE 3263793	G	850627	8527	
CA 1195614	A	851022	8547	
JP 91039267	B	910613	9128	

Priority Data (CC No Date): DE 3150596 (811221)

Applications (CC,No,Date): EP 82111801 (821220); JP 82222215 (821220)

Language: German

EP and/or WO Cited Patents: US 3522148; DE 2356493; DE 2316430; DE 1189763; DE 2356496

Designated States

(Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE

Abstract (Basic): In a new process for the prodn. of a tissue thromboplastin prepn. sensitive to clothing factor (VII) by prodn. of acetone dry powder from mammalian tissue and extn. of the powder with salt soln. the extn. is carried out with a salt soln. contg. 1-20 mmol ca ions per litre and, opt. a surfactant, and the extract is opt. dried.

The extn. is pref. performed with a soln. contg. 5-15 mmol calcium

(cont. next page)

ions oer litre, oref. in the form of a calcium salt of a water-soluble carboxylic acid. The extn. soln. advantageously additionally contains 0.01-0.5% of a surfactant.

The prod. is used for the diagnosis of blood coagulation disorders by means of the quick or prothrombin time-test. The new extn procedure is simple and avoids conditions which could damage the prothrombin. (16pp)

Abstract (EP): 8521 EP 83773

Process for the preparation of a tissue thromboplastin preparation, which is sensitive towards coagulation factor VII, by the

of the powder with salt solution, characterised in that one carries out the extraction with a salt solution which contains 1 to 20 mmol/l Ca ions and optionally a surface-active agent, and optionally dries the extract. @ (5pp) @

preparation

Derwent Class: B04; S03; R16;

Int Pat Class: C07G-007/00; G01N-033/86; C12Q-001/56; G01N-000/00; A61K-035/30; A61K-037/54; A23K-000/00; A61K-000/00; C07G-003/00; C07K-015/06

#### Record - 25

DIALOG(R) File 351:Derwent WPI

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003540340 WPI Acc No: 82-88332E/42

XRAM Acc No: C82-E88332

Reagent for optical determination of blood coagulation contains thrombin substrate, buffer and non proteolytic thromboplastin

Patent Assignee: (BOEF ) BOEHRINGER MANNHEIM GMBH

Author (Inventor): JERING H; BECKER U; ROESCHLAU P

Number of Patents: 011

Patent Family:

CC Number	Kind	Date	Week	
EP 62310	A	821013	8242	(Basic)
DE 3113350	A	821021	8243	
NO 8201101	A	821025	8246	
JP 57178161	A	821102	8249	
DK 8201519	A	830228	8315	
DD 202347	A	830907	8402	
US 4458015	A	840703	8429	
EP 62310	B	851211	8550	
DE 3267870	G	860123	8605	
CA 1198660	A	851231	8606	
JP 88056501	B	881108	8848	

Priority Data (CC No Date): DE 3113350 (810402)

Applications (CC,No,Date): US 360099 (820319); EP 82102773 (820401); JP 8253946 (820402)

Language: German

EP and/or WO Cited Patents: EP 14039; 2.Jnl.REF

Designated States

(Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE

Abstract (Basic): Reagent for optical determin. of blood coagulation (the Quick test) properties comprises (1) a synthetic thrombin substrate (I); (2) a buffer and (3) a thromboplastin (II) which has no proteolytic activity. (II) is prepd. from the 'acetone dry powder' (A) from brain by incubating an aq., neutral soln. of (A) at 25-40 deg.C, then recovering insolubles. These are suspended in dil. salt soln., treated with a surfactant in presence of a formate and the sepd.

(cont. next page)

soluble fraction dried. Pref. the reagent contains 3-20 vol.% (II); 20-200 micromoles per l (I); 0.05-0.25 moles per l pH 7.2-8.5 buffer; 2-10 mmoles per l Ca salt and opt. also 0.5-3% urea. The method is used e.g. to identify persons at risk from haemorrhage or thrombosis; to monitor anticoagulant therapy etc. This single component reagent is storage stable ((II) does not degrade (II)), gives reliable results and can be used in diluted form (to avoid turbidity problems) without excessively lengthening the test time. (15pp)

Abstract (US): 8429 US 4458015

Reagent for optical determin. of blood coagulation behaviour (Quick test) comprises thromboplastin, a synthetic thrombin substrate and a buffer of pH 7.2-8.5. The thromboplastin is non-protolytically active so as to develop only about 22.7-35.7% of the extinction at 405 nm as compared with normal thromboplastin when each is incubated at 20 deg.C with tris HCl buffer of pH 8.1 in the presence of a chromogeneous substrate for 1-7 days.

ADVANTAGE - The reagent contains all the required components, is storage stable and gives accurate results. @(5pp)@

Abstract (EP): 8550 EP 62310

Reagent for the optical determination of the blood coagulation behaviour (Quick test), containing thromboplastin, a synthetic thrombin substrate and buffer, characterised by a content of a non-proteolytically-active thromboplastin which is obtainable by preparation of an acetone dry powder from brain, incubation of a neutral aqueous solution of the acetone dry powder at 25 to 40 deg.C, obtaining of the insoluble fraction, treatment of a suspension of this fraction in dilute salt solution with a surface-active agent in the presence of formate and drying of the separated soluble fraction.

@(7pp)@

Derwent Class: B04; S03; S05; R16;

Int Pat Class: C12Q-001/56; G01N-033/86; C12Q-000/00; G01N-021/82;  
C12N-009/99

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DDDDDD II  AAAAAA LL      00000  GGGGG
DDDDDDD II  AAAAAAA LL     0000000 GGGGGGG
DD DD II AA  AA  LL      OO      OOGG  GG
DD DD II AA  AA  LL      OO      OG
DD DD II AA  AAAAAA LL      OO      OG  GGGG
DD DD II AA  AAAAAA LL      OO      OOGG  GG
DD DDDD II AA  AA  LLLLLLLLOOOOOOO GGGGGGG
DD DDD II AA  AA  LLLLLL 00000  GGGGG
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## File(s) searched:

File 155: MEDLINE(R) 1966-1994/Sep W2  
(c) format only 1994 Dialog Info.Svcs.  
File 73: EMBASE 1974-1994/ISS 29  
(c) 1994 Elsevier Science B.V.  
File 5: BIOSIS PREVIEWS(R) 1969-1994/Aug W1  
(c) 1994 BIOSIS  
File 399: CA Search(R) 1967-1994/UD=12102  
(c) 1994 American Chemical Society

## Sets selected:

Set	Items	Description
1	17104	THROMBOPLASTIN?
2	11833	PROTHROMBIN() TIME
3	4591	1 AND 2
4	152528	DRY
5	20	3 AND 4
6	3156	RECOMBINANT() TISSUE
7	21	3 AND 6
8	0	RECOMBINANT PROTEINS! FROM 155
9	40240	RECOMBINANT PROTEINS! FROM 155
10	36	3 AND 9
11	36454	RECOMBINANT() PROTEIN? ?
12	45	3 AND 11
13	1330027	DIAGNOSIS/DE
14	3	(S10 OR S12) AND DIAGNOSIS/DE
15	27952	STRIP
16	0	S3 AND STRIP
17	857974	TEST
18	964	S3 AND TEST
19	96	13 AND 18
20	667717	ASSAY?
21	19	S19 AND ASSAY?
22	40	5 OR 14 OR 21
23	28	RD (unique items)
24	28	Sort S23/ALL/PY,D

Prints requested : ('\*' indicates user print cancellation)

Date	Time	Description
20jul	11:30EST	P221: PR 24/5/ALL VIA MODEM (items 1-28 ADDR ADDEPTA)

Record - 1

DIALOG(R) File 73:EMBASE  
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9035741 EMBASE No: 93339469

A hexagonal (II) phase phospholipid neutralization assay for lupus anticoagulant identification

Triplett D.A.; Barna L.K.; Unger G.A.

Department of Pathology, Ball Memorial Hospital, 2401 University Avenue,  
Muncie IN 47303 USA

THROMB. HAEMOST. (Germany) , 1993, 70/5 (787-793) CODEN: THHAD ISSN:  
0340-6245

LANGUAGES: English SUMMARY LANGUAGES: English

SUBFILES: 025; 026

Lupus anticoagulants (LAs) are immunoglobulins (IgG, IgM, or both) which interfere with in vitro phospholipid (PL) dependent tests of coagulation (e.g. APTT, dilute PT, dilute Russell Viper Venom Time). These antibodies may be identified in a wide variety of clinical settings. With the exception of heparinized patient samples, the presence of LAs is often the most common cause of an unexplained APTT in a routine clinical laboratory. The diagnosis of LAs is difficult due to variable screening reagent sensitivity and intrinsic heterogeneity of LAs. Recently, Rauch and colleagues have shown human monoclonal hybridoma LAs were inhibited by hexagonal (II) phase PLs. In contrast, lamellar phase PLs had no effect. We have evaluated a new assay system, Staclo LA, which utilizes a hexagonal (II) phase PL (egg phosphatidylethanolamine (EPE)) as a confirmatory test for LAs. Plasma samples from the following patient populations were studied: LA positive, heparinized, oral anticoagulated, hemophilia A and B, and specific factor inhibitors, (factors V, VIII, IX). Unlike previous studies, the LA positive patients were a mixed population including: autoimmune diseases, drug-induced, and post-infection. Our findings confirm the specificity of hexagonal (II) phase PL neutralization of LAs.

EMTAGS:

Immunological procedures 0102; Congenital disorder 0315; Diagnosis 0140;

Mammal 0738; Human 0888; Clinical article 0152; Priority journal 0007;

Article 0060

DRUG DESCRIPTORS:

\*phospholipid--endogenous compound--ec; \*lupus anticoagulant--endogenous compound--ec

viper venom; phosphatidylethanolamine; heparin; blood clotting factor 8  
--endogenous compound--ec; blood clotting factor 5--endogenous compound--ec  
; blood clotting factor 9--endogenous compound--ec

MEDICAL DESCRIPTORS:

\*antibody detection

assay; partial thromboplastin time; prothrombin time; egg; anticoagulation;  
hemophilia a--diagnosis--di; hemophilia b--diagnosis--di; diagnostic  
accuracy; human; clinical article; priority journal; article

CAS REGISTRY NO.: 1405-71-6; 8057-48-5; 8065-01-8; 9005-48-5; 37187-54-5;  
9001-27-8; 9001-24-5; 9013-23-4; 9001-28-9

Record - 2

DIALOG(R) File 73:EMBASE  
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(cont. next page)

8862506 EMBASE No: 93166561

**Recombinant thromboplastin is slightly more sensitive to factor VII Padua**  
than standard thromboplastins of human origin (1)

Girolami A.; Sartori M.T.; Steffan A.; Fadin M.A.

University of Padua Medical School, Institute of Medical Semeiotics, IV

Department of Internal Medicine, Via Ospedale Civile 105, Padua Italy

BLOOD COAGUL. FIBRINOLYSIS (United Kingdom) , 1993, 4/3 (497-498)

CODEN: BLFIE ISSN: 0957-5235 ADONIS ORDER NUMBER: 095752359300103B

LANGUAGES: English

SUBFILES: 025

EMTAGS:

Diagnosis 0140; Etiology 0135; Congenital disorder 0315; Mammal 0738; Human

0888; Letter 0008

DRUG DESCRIPTORS:

\*blood clotting factor 7--endogenous compound--ec; \*thromboplastin; \*

recombinant protein

MEDICAL DESCRIPTORS:

\*prothrombin time; \*blood clotting disorder--diagnosis--di; \*blood clotting

disorder--etiology--et; \*blood clotting disorder--congenital disorder--cn

human; letter

CAS REGISTRY NO.: 9001-25-6; 9035-58-9

Record - 3

DIALOG(R) File 73:EMBASE

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8824080 EMBASE No: 93127887

Diagnosis of factor VIII versus nonspecific inhibitors

Goldsmith J.C.

Childrens Hematology/Oncology Ctr., Childrens Hospital Los Angeles, Mail

Stop 54, 4650 Sunset Blvd, Los Angeles, CA 90027 USA

SEMIN. HEMATOL. (USA) , 1993, 30/2 SUPPL. 1 (3-6) CODEN: SEHEA ISSN:

0037-1963

LANGUAGES: English

SUBFILES: 025

EMTAGS:

Diagnosis 0140; Etiology 0135; Therapy 0160; Congenital disorder 0315;

Mammal 0738; Human 0888; Priority journal 0007; Review 0001

DRUG DESCRIPTORS:

\*blood clotting factor 8 inhibitor--endogenous compound--ec; \*anticoagulant

agent--endogenous compound--ec

lupus anticoagulant--endogenous compound--ec; blood clotting factor 9

--endogenous compound--ec; blood clotting factor 11--endogenous compound

--ec; blood clotting factor 8--endogenous compound--ec

MEDICAL DESCRIPTORS:

\*laboratory test; \*blood clotting disorder--diagnosis--di; \*blood clotting

disorder--etiology--et

hemarthrosis--etiology--et; hemarthrosis--therapy--th; hemophilia a

--diagnosis--di; assay; partial thromboplastin time; prothrombin time;

thrombocyte count; bleeding time; fibrinolysis; human; priority journal;

review

CAS REGISTRY NO.: 9001-28-9; 9013-55-2; 9001-27-8

(cont. next page)

Record - 4

DIALOG(R) File 73:EMBASE  
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8801913 EMBASE No: 93105705

Autoantibody to von Willebrand factor in systemic lupus erythematosus  
Soff G.A.; Green D.  
Division of Hematology/Oncology, Northwestern Univ. Medical School,  
Searle Building 3-565, 303 East Chicago Ave., Chicago, IL 60611-3008 USA  
J. LAB. CLIN. MED. (USA), 1993, 121/3 (424-430) CODEN: JLCMA ISSN:  
0022-2143

LANGUAGES: English SUMMARY LANGUAGES: English

SUBFILES: 005; 013; 025; 026

A 17-year old woman (patient 1) was found to have severe bleeding as the initial manifestation of systemic lupus erythematosus. Profound deficiencies of factor VIII coagulation activity (10%) von Willebrand factor (vWF) antigen (<10%), and ristocetin cofactor (<1%), and a disproportionate loss of large molecular weight multimers of vWF were observed. An antibody to vWF was suspected, and an enzyme-linked immunoadsorbent assay (ELISA) was devised to detect and quantify such antibody. The ELISA measured the binding of anti-vWF antibody from sample plasma to surface-bound vWF antigen. Binding was detected by a conjugate of alkaline phosphatase with affinity-purified anti-human immunoglobulin G, A, or M and a chromogenic substrate for alkaline phosphatase. Controls included plasma from normal subjects, from patients with von Willebrand's disease, and from a patient (patient 2) with type III von Willebrand's disease who had developed an inhibitor to vWF. Analysis of our patient's plasma revealed immunoglobulin G, A, and M anti-vWF antibodies. Preincubation of the plasma from patient 1 and patient 2 with pure vWF antigen completely inhibited antibody binding, confirming antibody specificity. These antibodies were quantitatively titered by determining the volume ratio of normal pooled plasma (a source of vWF antigen) to test plasma required to inhibit 50% of the antibody binding to immobilized vWF antigen. The value was 0.8 plus or minus 0.3 (mean plus or minus SD of three determinations) for the immunoglobulin G of our patient as compared with 15.6 plus or minus 2.9 for the immunoglobulin G of patient 2. The titers of the immunoglobulin A and M were less than 0.05. Increases in factor VIII coagulant activity, vWF antigen, and ristocetin cofactor and control of hemorrhage could be transiently achieved by use of intravenous and intranasal desmopressin and the factor VIII concentrate Humate-P. Treatment with prednisone over an 8-month period led to a cessation of bleeding, restored normal levels of vWF and multimers, and decreased antibody titers. This study documented a case of acquired von Willebrand's disease caused by systemic lupus erythematosus and the development of an ELISA to detect and quantitate the presence of anti-von Willebrand factor antibody.

TRADE NAME/MANUFACTURER NAME: humate p/USA armour

EMTAGS:

Diagnosis 0140; Therapy 0160; Etiology 0135; Congenital disorder 0315;  
Immunological procedures 0102; Mammal 0738; Human 0888; Female 0042; Case  
report 0151; Controlled study 0197; Adolescent 0017; Oral and intragastric  
drug administration 0181; Intravenous drug administration 0182; Intranasal  
drug administration 0283; Priority journal 0007; Article 0060; Enzyme 0990  
DRUG DESCRIPTORS:

\*von willebrand factor--endogenous compound--ec; \*blood clotting factor 8  
--endogenous compound--ec; \*blood clotting factor 8 concentrate--drug  
administration--ad; \*blood clotting factor 8 concentrate--drug dose--do; \*

(cont. next page)



blood clotting factor 8 concentrate--drug therapy--dt; \*blood clotting factor 8 concentrate--pharmacology--pd; \*prednisone--drug dose--do; \*prednisone--drug therapy--dt; \*immunoglobulin a antibody--endogenous compound--ec; \*immunoglobulin m antibody--endogenous compound--ec; \*desmopressin--drug administration--ad; \*desmopressin--drug dose--do; \*desmopressin--drug therapy--dt; \*desmopressin--pharmacology--pd; \*immunoglobulin g antibody--endogenous compound--ec; \*immunoglobulin g antibody--pharmacology--pd  
alkaline phosphatase; autoantibody--endogenous compound--ec; tranexamic acid--drug administration--ad; tranexamic acid--drug dose--do; tranexamic acid--drug therapy--dt; adrenalin; collagen; adenosine diphosphate  
MEDICAL DESCRIPTORS:  
\*systemic lupus erythematosus--diagnosis--di; \*systemic lupus erythematosus--drug therapy--dt; \*bleeding--drug therapy--dt; \*bleeding--etiology--et; \*von willebrand disease--complication--co; \*von willebrand disease--diagnosis--di  
enzyme linked immunosorbent assay; antigen binding; symptomatology; prothrombin time; partial thromboplastin time; bleeding time; thrombocyte aggregation; thrombocyte agglutination; human; female; case report; controlled study; adolescent; oral drug administration; intravenous drug administration; intranasal drug administration; priority journal; article  
EMCLAS DRUG CODES:  
03700000000

CAS REGISTRY NO.: 109319-16-6; 9001-27-8; 53-03-2; 16679-58-6; 9001-78-9; 701-54-2; 1197-18-8; 51-43-4; 55-31-2; 6912-68-1; 9007-34-5; 58-64-0; 20398-34-9

Record - 5

DIALOG(R) File 155:MEDLINE(R)  
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08711286 94026286  
[Antithrombotic and antiplatelet effects of rosmarinic acid, a water-soluble component isolated from radix Salviae miltiorrhizae (danshen)]  
Zou ZW; Xu LN; Tian JY  
Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing.  
Yao Hsueh Hsueh Pao (CHINA) 1993, 28 (4) p241-5, ISSN 0513-4870  
Journal Code: 1PU  
Languages: CHINESE Summary Languages: ENGLISH  
Document type: JOURNAL ARTICLE English Abstract  
JOURNAL ANNOUNCEMENT: 9401  
Subfile: INDEX MEDICUS  
Wistar rats of both sex were used. Ros A was intravenously injected 5-10 min before blood collection or the ligation of vena cava. 1. Stasis-induced venous thrombosis: A tight ligature was applied to inferior vena cava below the left renal vein in anesthetized rats. The abdominal walls were closed and then reopened two hours later. The vena cava was clamped 2 cm below the ligature. This segment was cut to remove the thrombus. The dry weight of the thrombus was determined. 2. Platelet aggregation: Using Born's method the platelet aggregation induced by collagen or ADP was studied. 3. Blood coagulation times: Blood recalcium time (RT), kaolin partial thromboplastin time (KPTT) and prothrombin time (PT) were estimated. 4. Plasma fibrinolytic activity was observed by the determination of euglobulinolytic time (ELT). Plasma fibrinogen content was estimated based on the biuret reaction. The venous thrombosis was inhibited by 41.9% and 54.8% (P < 0.05)

(cont. next page)

when Ros A was injected at the dosages of 50 and 100 mg/kg. The blood platelet aggregation elicited by collagen was suppressed by 30.4% (P < 0.05) and 46.4% (P < 0.01) after the injection of Ros A at doses of 100 and 150 mg/kg respectively. The ELT was shortened after the injection of Ros A (100 and 150 mg/kg) as compared with the control value (P < 0.05), while the plasma fibrinogen content remained unchanged. The results that Ros A showed mild antithrombotic effect. The mechanism of this effect might be related to its inhibition of platelet aggregation and promotion of fibrinolytic activity.

Tags: Animal; Female; Male

Descriptors: \*Cinnamates--Pharmacology--PD; \*Platelet Aggregation--Drug Effects--DE; \*Platelet Aggregation Inhibitors--Pharmacology--PD; \*Venae Cavae; Blood Coagulation Tests; Cinnamates--Therapeutic Use--TU; Fibrinogen--Metabolism--ME; Platelet Aggregation Inhibitors--Therapeutic Use--TU; Rats; Rats, Wistar; Thrombosis--Prevention and Control--PC

CAS Registry No.: 0 (Cinnamates); 0 (Platelet Aggregation Inhibitors); 537-15-5 (rosmarinic acid); 9001-32-5 (Fibrinogen)

#### Record - 6

DIALOG(R) File 155:MEDLINE(R)

(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

08690539 94005539

Coagulation tests in predicting haemorrhage after prostatic resection.

Ahsan Z; Cartner R; English PJ

Department of Urology, Dryburn Hospital, Durham.

Br J Urol (ENGLAND) Aug 1993, 72 (2) p201-6, ISSN 0007-1331

Journal Code: B3K

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9401

Subfile: INDEX MEDICUS

It is known that disseminated intravascular coagulation (DIC) can contribute towards blood loss after transurethral resection of the prostate because of the absorption of various prostatic substances. The aim of the present study was to establish whether simple coagulation tests (prothrombin time/activated partial thromboplastin time) carried out immediately after surgery would be useful in predicting those patients who bleed excessively after prostatic resection due to DIC. Criteria to determine significant post-operative haemorrhage were defined. Of 110 patients entered into the study, 34.5% had significant post-operative bleeding and 74% of these had an abnormal prothrombin time (> or = 15 s) immediately after surgery. An abnormal prothrombin time was associated with the resection of large prostates but could also predict the risk of bleeding independent of the resected weight; 18% of patients with an abnormal prothrombin time were also found to have an abnormal activated partial thromboplastin time and all of these had significant blood loss. A group of patients with an abnormal prothrombin time and a resected dry weight > or = 35 g was identified as a high risk group.

Tags: Human; Male

Descriptors: \*Disseminated Intravascular Coagulation--Etiology--ET; \*Hematuria--Etiology--ET; \*Prostatectomy--Adverse Effects--AE; \*Prostatic Diseases--Surgery--SU; Aged; Aged, 80 and over; Disseminated Intravascular Coagulation--Prevention and Control--PC; Hematuria--Prevention and Control--PC; Middle Age; Partial Thromboplastin Time; Postoperative Period; Prospective Studies; Prostate--Pathology--PA; Prostatic Diseases--Pathology--PA; Prothrombin Time

(cont. next page)

Record - 7

DIALOG(R) File 155:MEDLINE(R)

(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

08567319 93277319

Decentralized testing for prothrombin time and activated partial thromboplastin time using a dry chemistry portable analyzer.

Rose VL; Dermott SC; Murray BF; McIver MM; High KA; Oberhardt BJ  
Center for Thrombosis and Hemostasis, University of North Carolina, Chapel Hill.

Arch Pathol Lab Med (UNITED STATES) Jun 1993, 117 (6) p611-7, ISSN 0003-9985 Journal Code: 79Z

Contract/Grant No.: R44HL37174, HL, NHLBI; 5-K08-HL01922, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9309

Subfile: AIM; INDEX MEDICUS

Previous work has established the precision and accuracy of a portable blood coagulation analysis system using paramagnetic particles contained in a dry reagent on a disposable test card. We examined the deployment of this technology in decentralized hospital settings and compared test results obtained in the surgical intensive care unit, coronary care unit, and outpatient cardiology clinic with those obtained in the central laboratory. Nursing personnel were instructed in the use of the system, and quality control testing was performed daily by the laboratory staff. In the intensive care units, patient subjects included those on whom tests of prothrombin time and activated partial thromboplastin time had been ordered. Immediate determinations were performed by the intensive care unit nursing staff on the same citrated, whole-blood samples that were subsequently sent to the central laboratory. In the outpatient cardiology clinic, fingerstick blood samples were obtained for prothrombin time determinations with the dry chemistry system. Paired prothrombin time samples obtained by venipuncture were run in the hospital laboratory. The study involved multiple users, multiple locations, two lots of activated partial thromboplastin time cards, and several different instruments, over an extended period. Correlation coefficients between the dry chemistry system and the hospital laboratory under these conditions were in an acceptable range in all sites studied. We concluded that, with appropriate training and quality assurance, the dry chemistry system provides an acceptable alternative to the hospital laboratory for prothrombin time and activated partial thromboplastin time determinations.

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: \*Chemistry, Analytical--Instrumentation--IS; \*Chemistry, Analytical--Methods--MT; \*Partial Thromboplastin Time; \*Prothrombin Time; Diagnosis, Computer-Assisted; Evaluation Studies; Fibrinogen--Analysis--AN; Osmolar Concentration

CAS Registry No.: 9001-32-5 (Fibrinogen)

Record - 8

DIALOG(R) File 5:BIOSIS PREVIEWS(R)

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10058382 BIOSIS Number: 95058382

COMPARATIVE EVALUATION OF COAGULATION QUALITY CONTROL PLASMAS

FAVALORO E J; GRISPO L; EXNER T

HAEMOSTASIS AND THROMBOSIS UNIT, SPECIAL COAGULATION LAB., HAEMATOL.

(cont. next page)

DEP., INST. CLINICAL PATHOL. AND MED. RES., WESTMEAD HOSP., WESTMEAD NSW  
2145.

AUST J MED SCI 13 (4). 1992. 158-169. CODEN: AUJME

Language: ENGLISH

Quality control (QC) plasma samples from 9 separate coagulation supply companies, and comprising both normal and abnormal QC samples, have been evaluated by us in a comparative study. Samples were tested in parallel for behaviour in both prothrombin time (PT) and activated partial thromboplastin time (APTT) assays in regard to various parameters, including precision, stability following reconstitution, and for storage stability (using dry storage at 37.degree.C to mimic longer term storage under more optimal conditions). Whilst most plasma samples performed adequately in our study, some yielded less acceptable results. Inter-run precision for all QC 'normal' plasmas was such that coefficients of variation (CV) were in the vicinity of 2-3%, as were CV's for 'in-house' study control plasmas. CV's obtained for 'abnormal' QC plasma samples were generally higher (3-12%). Most (but not all) QC plasmas showed notable signs of deterioration following storage of dry vials at 37.degree.C for 1 or 2 months. Most (but not all) QC plasma samples (both 'normal' and 'abnormal') showed an acceptable level of stability following reconstitution (tested over a 24 hour period). Interestingly, stability appeared to be better for some QC plasmas (particularly 'normals') when held at room temperature following reconstitution rather than at 4.degree.C. Whilst the general trend for most QC plasmas was an upward drift in PT/APTT with time, some plasmas actually showed a downward trend. In an attempt to explain some of these findings, and to help provide reasons for discrepancies observed in the behaviour of different QC plasmas, measurements for pH, refractive index, estimates of turbidity and dry matter weights have also been undertaken and data compared.

Descriptors/Keywords: HUMAN QUALITY ASSURANCE BLOOD COAGULATION TEST

Concept Codes:

- \*01004 Methods, Materials and Apparatus, General-Laboratory Methods
- \*15001 Blood, Blood-Forming Organs and Body Fluids-General; Methods
- \*15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
- 15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies

Biosystematic Codes:

86215 Hominidae

Super Taxa:

Animals; Chordates; Vertebrates; Mammals; Primates; Humans

#### Record - 9

DIALOG(R)File 73:EMBASE

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8556589 EMBASE No: 92232828

Reversible prothrombin time prolongation after plasma storage on dry ice  
(2)

Plumhoff E.A.; Fisher P.K.; Bowie E.J.W.; Nichols W.L.

General Laboratory, Mayo Clinic, Rochester, MN USA

THROMB. HAEMOSTASIS (Germany), 1992, 68/2 (232) CODEN: THHAD ISSN:  
0340-6245

LANGUAGES: English

SUBFILES: 025; 027

EMTAGS:

Mammal 0738; Human 0888; Priority journal 0007; Letter 0008

DRUG DESCRIPTORS:

(cont. next page)

\*carbon dioxide

**MEDICAL DESCRIPTORS:**

\*prothrombin time; \*blood storage; \*partial thromboplastin time  
human; priority journal; letter

CAS REGISTRY NO.: 124-38-9; 58561-67-4

**Record - 10**

DIALOG(R) File 73:EMBASE

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8523936 EMBASE No: 92199858

The precision of duplicate prothrombin time and partial thromboplastin time assays in neonates

DePalma L.; Rush R.A.; Luban N.L.C.

Department of Laboratory Medicine, Children's National Medical Center,  
111 Michigan Avenue NW, Washington, DC 20010 USA

ARCH. PATHOL. LAB. MED. (USA), 1992, 116/6 (657-659) CODEN: ARPAA

ISSN: 0003-9985

LANGUAGES: English SUMMARY LANGUAGES: English

SUBFILES: 007; 025; 029

An evaluation of duplicate prothrombin time (PT) and activated partial thromboplastin time (PTT) assays was performed in 277 neonatal samples. Performance criteria were analyzed to determine whether single vs duplicate procedures could be utilized reliably without exposing the neonates to the risk of erroneous PT and PTT results. In addition, we evaluated whether this approach might decrease phlebotomy and hence reduce the number of blood transfusions administered. For PT assays, 97.5% (270/277) of the duplicate results were different by 1 second or less. Only 2.5% (7/277) differed by 3 seconds. For PTT duplicates, 75.0% (207/277) of the values were different by 2 seconds or less and 13.0% (36/277) by 2 to 4 seconds. An additional 12.3% (34/277) were discrepant by as many as 4 seconds. The largest discrepancies occurred in specimens with markedly elevated PT and PTT results, indicative of a significant coagulopathy. In addition, heparin neutralization was performed successfully in 22 neonatal blood specimens showing either partial or full correction of PTT values due to heparin specimen contamination. This study indicates that single PT and PTT assays as well as heparin neutralization tests can be accurately performed and may be able to reduce blood donor exposure by as many as one blood transfusion every 2 to 3 days of hospitalization.

**EMTAGS:**

Diagnosis 0140; Therapy 0160; Mammal 0738; Human 0888; Normal humans 0800;  
Newborn 0013; Infant 0014; Child 0022; Priority journal 0007; Article 0060

**DRUG DESCRIPTORS:**

heparin

**MEDICAL DESCRIPTORS:**

\*prothrombin time; \*partial thromboplastin time; \*neonatology  
diagnostic test; blood clotting parameters; assay; phlebotomy; blood  
transfusion; diagnostic error; blood clotting disorder--diagnosis--di;  
human; normal human; newborn; priority journal; article

CAS REGISTRY NO.: 8057-48-5; 8065-01-8; 9005-48-5; 9005-49-6; 37187-54-5

**Record - 11**

DIALOG(R) File 73:EMBASE

(cont. next page)

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8409286 EMBASE No: 92085092

In vitro inhibition of blood coagulation by tripeptide aldehydes - a retrospective screening study focused on the stable D-MePhe-Pro-Arg-H.H2SO4 Bagdy D.; Barabas E.; Bajusz S.; Szell E.

Coagulation Labs, Institute for Drug Research, P.O. Box 82, H-1325 Budapest Hungary

THROMB. HAEMOSTASIS (Germany) , 1992, 67/3 (325-330) CODEN: THHAD

ISSN: 0340-6245

LANGUAGES: English SUMMARY LANGUAGES: English

SUBFILES: 025; 030

A series of peptide aldehydes synthesized in our institute during the last 15 years coagulation. Simple conventional clotting assays, platelet function tests and fibrinolytic methods were used to evaluate the inhibitory potency of the compounds in complex clotting systems as well as their supposed antifibrinolytic effect in vitro. Special attention was paid to the possible interactions with blood cells and plasma proteins, and to the functional stability of the inhibitors in several tissue homogenates. D-Phe-Pro-Arg-H (GYK1-14166, RGH-2958), Boc-D-Phe-Pro-Arg-H (GYK1-14451) and D-MePhe-Pro-Arg-H (GYK1-14766) were found to be the most potent inhibitors. The peptide aldehydes via formation of reversible complexes with thrombin impede the enzyme to react with the coagulation factors, platelet membrane and vessel wall. The compounds inhibit platelet aggregation induced by thrombin specifically without changing the sensitivity of platelets to other inducers. D-Phe-Pro-Arg-H and D-MePhe-Pro-Arg-H showed no antifibrinolytic effect. D-MePhe-Pro-Arg-H and BocD-Phe-Pro-Arg-H proved to be stable in dry state for years and in solution at room temperature for several days. The anticoagulant activity of the compounds was declared in NIH antithrombin units.

TRADE NAME/MANUFACTURER NAME: gyki 14166; rgh 2958; gyki 14451

EMTAGS:

Blood and hemopoietic system 0927; Cardiovascular system 0920; Dog 0711; Mammal 0738; Rabbits and hares 0731; Human 0888; Nonhuman 0777; Human tissue, cells or cell components 0111; Animal tissue, cells or cell components 0105; Priority journal 0007; Article 0060; Therapy 0160; Enzyme 0990

DRUG DESCRIPTORS:

\*tripeptide derivative--drug comparison--cm; \*tripeptide derivative--drug development--dv; \*tripeptide derivative--drug interaction--it; \*tripeptide derivative--pharmacology--pd  
tripeptide; aldehyde--pharmacology--pd; plasma protein--drug interaction--it; plasma protein--endogenous compound--ec; thrombin--endogenous compound--ec; blood clotting factor--endogenous compound--ec; heparin--drug comparison--cm; dextro phenylalanylprolylargininal--drug comparison--cm; dextro phenylalanylprolylargininal--drug development--dv; dextro phenylalanylprolylargininal--drug interaction--it; dextro phenylalanylprolylargininal--pharmacology--pd; unclassified drug

MEDICAL DESCRIPTORS:

\*blood clotting  
drug screening; thrombocyte function; fibrinolysis; blood cell; complex formation; enzyme inhibition; thrombocyte membrane; blood vessel wall; thrombocyte aggregation; drug stability; anticoagulation; dog; rabbit; blood clotting time; dose time effect relation; partial thromboplastin time; prothrombin time; thrombin time; human; nonhuman; human cell; animal cell; priority journal; article

(cont. next page)

DRUG TERMS (UNCONTROLLED): tert butyloxycarbonyl dextro  
phenylalanylprolylarginine--drug development--dv; tert butyloxycarbonyl  
dextro phenylalanylprolylarginine--drug interaction--it; tert  
butyloxycarbonyl dextro phenylalanylprolylarginine--pharmacology--pd  
EMCLAS DRUG CODES:  
03700000000

CAS REGISTRY NO.: 60503-05-1; 83997-16-4; 9002-04-4; 8057-48-5; 8065-01-8;  
9005-48-5; 9005-49-6; 37187-54-5; 69201-89-4

Record - 12

DIALOG(R) File 155:MEDLINE(R)  
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08205049 92343049  
Diagnostic efficacy of the D-dimer assay in disseminated intravascular  
coagulation (DIC).  
Bick RL; Baker WF  
Regional Cancer and Blood Disease Center of Kern, California.  
Thromb Res (UNITED STATES) Mar 15 1992, 65 (6) p785-90, ISSN  
0049-3848 Journal Code: VRN  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9210

Subfile: INDEX MEDICUS  
The D-Dimer (D-D) assay for measuring cross-linked fibrin degradation  
products is now available for the clinical laboratory. We combined this  
assay with other tests to assess patients with diagnosed or suspected DIC.  
Also, a small group of patients (20) with deep venous thrombosis (DVT) were  
studied. The D-D test, antithrombin-III assay, FDP titer, fibrinopeptide-A  
level, protamine sulfate test, fibrinogen, prothrombin time, and activated  
partial thromboplastin time were used. The D-D test was abnormal in 93.7%,  
the AT-III level was abnormal in 87.5%, the fibrinopeptide-A level was  
abnormal in 89.5%, and the FDP titer was elevated in 83.7% of patients with  
DIC. When assessing patients found not to have confirmed DIC the D-D assay  
was abnormal in 20%, the AT-III level was abnormal in 6%, and the  
fibrinopeptide-A level was elevated in 13%. We conclude the D-Dimer assay  
to be a useful molecular marker of hemostasis in diagnosing DIC and this  
test will often discriminate between those patients with or without DIC,  
especially when used with the AT-III and fibrinopeptide-A assays. Of the  
battery of tests used in this study, the most useful, in descending order  
of efficacy, appear to be the D-dimer assay (93.7% abnormal), the  
fibrinopeptide-A titer (89.5% abnormal), the AT-III level (87.5% abnormal),  
and the FDP titer (83.7% abnormal). Of the global tests, the diagnostic  
efficacy of the prothrombin time activated partial thromboplastin time, and  
protamine sulfate test were no greater than chance and appear to be of  
little use in aiding in a diagnosis of DIC. Also, the D-Dimer assay is  
similar in cost to the FDP titer and is cost effective for the routine  
clinical laboratory.

Tags: Human  
Descriptors: \*Disseminated Intravascular Coagulation--Diagnosis--DI;  
\*Fibrin Fibrinogen Degradation Products--Analysis--AN; Disseminated  
Intravascular Coagulation--Blood--BL; Predictive Value of Tests;  
Thrombophlebitis--Blood--BL  
CAS Registry No.: 0 (fibrin fragment D); 0 (Fibrin Fibrinogen  
Degradation Products)

(cont. next page)

Record - 13

DIALOG(R) File 155:MEDLINE(R)

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08184871 92322871

Exploration of rapid bedside monitoring of coagulation and fibrinolysis parameters during thrombolytic therapy.

Sane DC; Gresalfi NJ; Enney-O'Mara LA; Califf RM; Greenberg CS; Bovill EG; Oberhardt BJ

Department of Medicine, Duke University Medical Center, Durham, NC 27710.  
Blood Coagul Fibrinolysis (ENGLAND) Feb 1992, 3 (1) p47-54, ISSN 0957-5235 Journal Code: A5J

Languages: ENGLISH

Document type: CLINICAL TRIAL; JOURNAL ARTICLE; MULTICENTER STUDY

JOURNAL ANNOUNCEMENT: 9210

Subfile: INDEX MEDICUS

Monitoring coagulation parameters during thrombolytic therapy could be useful for prediction and treatment of haemorrhagic episodes. Technology based on dry reagent chemistry has been developed that allows rapid (less than 10 min) assays on small samples of whole blood. The assay principle is based on the restriction of motion of paramagnetic particles during fibrin polymerization, and subsequent liberation of particle motion during fibrinolysis. This technology was used to monitor prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen levels and fibrinolysis profiles during thrombolytic therapy with tissue plasminogen activator for acute myocardial infarction. The PT and aPTT obtained with the COAG-1 correlated well with conventional assays ( $r = 0.93$  and  $0.92$  for PT and aPTT, respectively;  $p = 0.0001$ ). Fibrinogen estimates, obtained by COAG-2 also correlated well with modified Clauss assays ( $r = 0.86$ ,  $p = 0.0001$ ). The rapid determination of the aPTT may improve management of adjunctive anticoagulant therapy following thrombolysis. The fibrinolysis profile may be useful during thrombolytic therapy to verify that a lytic state has been achieved, to monitor the lytic state throughout therapy, and to verify that the lytic state normalizes once therapy has been completed.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: \*Blood Coagulation--Physiology--PH; \*Fibrinolysis --Physiology--PH; \*Monitoring, Physiologic--Methods--MT; \*Thrombolytic Therapy; Blood Coagulation Tests; Fibrinogen--Metabolism--ME; Hemorrhage --Chemically Induced--CI; Hemorrhage--Diagnosis--DI; Hemorrhage --Drug Therapy--DT; Partial Thromboplastin Time; Pilot Projects; Prothrombin Time; Thrombolytic Therapy--Adverse Effects--AE; Time Factors

CAS Registry No.: 9001-32-5 (Fibrinogen)

Record - 14

DIALOG(R) File 155:MEDLINE(R)

(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

08173851 92311851

Recombinant tissue factor as substitute for conventional thromboplastin in the prothrombin time test.

Tripodi A; Arbini A; Chantarangkul V; Mannucci PM

A. Bianchi Bonomi Hemophilia and Thrombosis Center, IRCCS Maggiore Hospital and University, Milano, Italy.

Thromb Haemost (GERMANY) Jan 23 1992, 67 (1) p42-5, ISSN 0340-6245

Journal Code: VQ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

(cont. next page)



JOURNAL ANNOUNCEMENT: 9210

Subfile: INDEX MEDICUS

Relipidated recombinant tissue factor (r-TF) has been assessed in comparison with conventional rabbit brain thromboplastin (Manchester Reagent) for its suitability for measurement of prothrombin time (PT). The International Sensitivity Index (ISI) of r-TF calibrated against the International Reference Preparation BCT/253 (human plain) was found to be 0.96 and 1.12 with instrumental and manual techniques. Our study of plasmas from patients with congenital deficiencies of clotting factors covering a wide range of severity demonstrates that r-TF is able to detect even minor deficiencies of factors involved in the extrinsic and common coagulation pathways. Patients with liver diseases were correctly diagnosed with a

reproducibility expressed as coefficient of variation was 2.3% and 3.9% at normal and abnormal PT levels. In conclusion, our evaluation shows that relipidated r-TF possesses the necessary requisites of sensitivity, diagnostic accuracy and reproducibility which make it a suitable candidate for PT determination both for monitoring oral anticoagulant therapy and diagnosing congenital and acquired clotting factor deficiencies. Moreover, being a highly defined reagent it may constitute a step forward in the standardization of PT testing. prevalence of

Tags: Human

Descriptors: \*Prothrombin Time; Anticoagulants--Adverse Effects--AE; Blood Coagulation Disorders--Diagnosis--DI; Blood Coagulation Disorders--Etiology--ET; Evaluation Studies; Indicators and Reagents--Standards--ST; Liver Diseases--Blood--BL; Liver Diseases--Complications--CO; Recombinant Proteins; Reference Standards; Reproducibility of Results; Thromboplastin--Standards--ST

CAS Registry No.: 0 (Anticoagulants); 0 (Indicators and Reagents); 0 (Recombinant Proteins); 9035-58-9 (Thromboplastin)

Record - 15

DIALOG(R) File 5:BIOSIS PREVIEWS(R)  
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9088239 BIOSIS Number: 93073239

PROTEIN S ACTIVITY IN PATIENTS WITH HEREDOFAMILIAL PROTEIN S DEFICIENCY AND IN PATIENTS WITH JUVENILE VENOUS THROMBOSIS RESULTS OF A FUNCTIONAL METHOD

MACCAFERRI M; LEGNANI C; PREDA L; PALARETI G  
DEP. ANGIOLOGY BLOOD COAGULATION DISEASE, UNIVERSITY HOSP. S. ORSOLA, BOLOGNA, ITALY.

THROMB RES 64 (6). 1991. 647-658. CODEN: THBRA

Full Journal Title: Thrombosis Research

Language: ENGLISH

Using an ACL 300 R coagulometer (Instrumentation Laboratory) we assessed the clinical usefulness of a new method to measure PS activity (PS:Act), based on the prolongation of prothrombin time of a mixture of diluted plasma sample, PS depleted plasma previously incubated with Protac for protein C activation, bovine thromboplastin and calcium ions. The results were compared with those from immunological assays. PS:Act was measured in 42 apparently healthy subjects, in 12 patients with hereditary PS deficiency (HPSD group) diagnosed on the basis of immunologic tests and in 48 patients with episodes of juvenile venous thromboembolism at least three months prior to testing (JVTE group). All the HPSD patients had PS:Act below the normal range (< 62%). In JVTE group 9 patients (18.7%) showed abnormal results for PS:Act, 4 (8.3%) had low levels of free PS:Ag; all patients had normal total PS:Ag levels. Levels of antiphospholipid

(cont. next page)

antibodies (immunologic test) were normal in the 9 JVTE patients with low PS:Act. When all the results were considered together (n = 102), the correlation coefficient between PS:Act and free PS:Ag was 0.78 (p < 0.01).

Descriptors/Keywords: HUMAN INHERITED DEFECTS ACL 300R COAGULOMETER  
PROTHROMBIN PROTEIN C DIAGNOSIS THROMBOEMBOLISM ANTIPHOSPHOLIPID  
ANTIBODIES

Concept Codes:

\*02508 Cytology and Cytochemistry-Human  
\*03508 Genetics and Cytogenetics-Human  
\*12504 Pathology, General and Miscellaneous-Diagnostic  
\*14508 Cardiovascular System-Blood Vessel Pathology  
\*15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph  
Studies  
\*15006 Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and  
Reticuloendothelial Pathologies  
\*25000 Pediatrics  
\*34502 Immunology and Immunochemistry-General; Methods  
0064 Biochemical Studies-Proteins, Peptides and Amino Acids 10068 Biochemical St  
10504 Biophysics-General Biophysical Techniques  
Biosystematic Codes:  
86215 Hominidae  
Super Taxa:  
Animals; Chordates; Vertebrates; Mammals; Primates; Humans

Record - 16

DIALOG(R) File 73:EMBASE  
(c) 1994 Elsevier Science B.V. All rts. reserv.

8101465 EMBASE No: 91133319  
Assays for lupus anticoagulant: The sensitivity of different assays  
Jain A.; Dash S.; Marwaha N.; Deodhar S.D.; Sehgal S.  
Department of Haematology, Postgraduate Institute of Medical Education  
and Research, Chandigarh 160 012 India  
MED. LAB. SCI. (United Kingdom), 1991, 48/1 (31-35) CODEN: MLASD  
ISSN: 0308-3616 ADONIS ORDER NUMBER: 0308361691000367  
LANGUAGES: English  
SUBFILES: 025; 029; 031

Fifty patients with systemic lupus erythematosus were studied for the  
presence of lupus anticoagulant using three different assays - kaolin  
clotting time, platelet neutralization test, and tissue thromboplastin  
inhibition test. Lupus anticoagulant could be detected in seven cases (14%)  
with the use of one test in cases with a partial prothrombin time with  
kaolin more than five seconds greater than normal. The detection rate rose  
to 20% (10 cases) when using all three tests, so a panel of three assays  
could identify lupus patients apparently at risk for thrombotic  
complications.

EMTAGS:

Diagnosis 0140; Mammal 0738; Human 0888; Human tissue, cells or cell  
components 0111; Clinical article 0152; Priority journal 0007; Article 0060

DRUG DESCRIPTORS:

\*anticoagulant agent--endogenous compound--ec

MEDICAL DESCRIPTORS:

\*systemic lupus erythematosus--diagnosis--di; \*blood clotting factor  
assay; human; human tissue; clinical article; priority journal; article

(cont. next page)

Record - 17

DIALOG(R) File 155:MEDLINE(R)

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07680391 91199391

Dry reagent technology for rapid, convenient measurements of blood coagulation and fibrinolysis.

Oberhardt BJ; Dermott SC; Taylor M; Alkadi ZY; Abruzzini AF; Gresalfi NJ  
Cardiovascular Diagnostics, Inc., Research Triangle Park, NC 27709.

Clin Chem (UNITED STATES) Apr 1991, 37 (4) p520-6, ISSN 0009-9147

Journal Code: DBZ

Contract/Grant No.: R44HL37174, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9107

Subfile: INDEX MEDICUS

Rapid coagulation and fibrinolysis assays suitable for use with an imprecisely measured sample volume (either whole blood or plasma) have been developed, utilizing a technology based on paramagnetic iron oxide particles (PIOp) that move in response to an oscillating magnetic field. PIOp are combined with appropriate test reagents for clotting and thrombolysis assays and formulated as dry reagents within a capillary test chamber. The minima and maxima of the PIOp oscillations define a two-sided waveform that provides kinetic information on fibrin polymerization and lysis. Subject to the chemistry of the dry reagent formulation, the resulting waveform can be used to define clotting time, lysis onset time, or fibrinogen variables. Applications to one-stage prothrombin time and one-stage activated partial thromboplastin time tests have yielded assays with consistently good correlations with other test methods. Applications to fibrinolysis studies have yielded global assays of thrombolytic activity, in that the assay results reflect the interactions of multiple factors associated with the effectiveness of thrombolytic therapy. Depending on the components utilized in a particular reagent formulation, one can derive information about the activity of such factors as fibrinogen, plasminogen, and related inhibitors, as well as the lytic agent being administered. Use of these assays in a clinical setting should provide a rapid, convenient alternative to conventional testing of coagulation variables and a reliable method for monitoring thrombolytic therapy.

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: \*Blood Coagulation Tests; \*Fibrinolysis; Chemistry, Clinical

--Instrumentation--IS; Ferric Compounds; Microcomputers; Prothrombin Time

CAS Registry No.: 0 (Ferric Compounds); 1309-37-1 (ferric oxide)

Record - 18

DIALOG(R) File 73:EMBASE

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7434906 EMBASE No: 89157129

The incidence and significance of hemostatic abnormalities in patients with head injuries

Olson J.D.; Kaufman H.H.; Moake J.; O'Gorman T.W.; Hoots K.; Wagner K.; Kice Brown C.; Gildenberg P.L.

Department of Pathology, University of Iowa College of Medicine, Iowa City, IA 52242 USA

NEUROSURGERY (USA), 1989, 24/6 (825-832) CODEN: NRSRD ISSN: 0148-396X

LANGUAGES: English

(cont. next page)

SUBFILES: 008; 025

Abnormal coagulation and fibrinolysis is a frequent complication in patients with head injury. This complication can be severe enough to lead to hemorrhage or thrombosis. A study was undertaken to determine if the hemostatic abnormalities are reliable indicators of outcome. Hemostasis in 269 patients with head injuries alone was screened using platelet count (PC), prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin clotting time (TCT), fibrinogen assay (FIB), level of fibrin-fibrinogen degradation products (FDP), and disseminated intravascular coagulation (DIC) score in the first 24 hours after injury. Test results were compared with the outcome (discharged or dead) in the entire group and in subgroups divided on the basis of the severity of injury as determined by the Glasgow coma score (GCS). Increased consumptive coagulopathy at admission, as reflected in the DIC score, predicts the outcome of head-injured patients with a high degree of accuracy. The degree of increase of the initial FDP level and prolongation of TCT also correlated positively with the outcome. Prolongation of the APTT correlated strongly with unfavorable outcome in a large group of patients, and in a small group, markedly accelerated APTT also predicted death. Stepwise logistic regression analysis demonstrated that GCS, FDP level, and DIC score predicted outcome. Other tests did not provide additional predictive value. Abnormal hemostasis frequently complicates the course of patients with head injuries. This study demonstrates that hemostasis tests are predictors of outcome in these patients.

EMTAGS:

Trauma 0301; Diagnosis 0140; Blood and hemopoietic system 0927; Adolescent 0017; Aged 0019; Child 0022; Adult 0018; Major clinical study 0150; Human 0888; Fatality 0171; Immunological procedures 0102; Priority journal 0007

MEDICAL DESCRIPTORS:

\*head injury--diagnosis--di; \*hemostasis; \*disseminated intravascular clotting--diagnosis--di; \*fibrinolysis--diagnosis--di; \*blood clotting adolescent; aged; child; adult

Record - 19

DIALOG(R)File 73:EMBASE

(c) 1994 Elsevier Science B.V. All rts. reserv.

7360868 EMBASE No: 89077014

Postoperative bleeding in cardiovascular surgery. Does heparin rebound really exist?

Gundry S.R.; Drongowski R.A.; Klein M.D.; Coran A.G.

Section of Thoracic Surgery, Department of Surgery, University of Michigan Hospitals, Ann Arbor, MI USA

AM. SURG. (USA), 1989, 55/3 (162-165) CODEN: AMSUA ISSN: 0003-1348

LANGUAGES: English

SUBFILES: 009; 025; 029

Postoperative bleeding following cardiovascular procedures is troublesome and often life-threatening. The effect of heparin (H) is usually reversed with protamine sulfate (P) at the end of vascular procedures; subsequent bleeding or abnormal coagulation times are ascribed to so-called heparin rebound and are treated with extra empiric doses of P. H rebound has heretofore been described only by using biologic clotting test, which are often abnormal postoperatively. Thus, many instances of postoperative bleeding are treated with inappropriate and dangerous doses of P in the mistaken impression that more H needs to be reversed. Using the new test for plasma H, the azure A Assay, which measured H chemically rather than biologically, 27 patients were tested after cardiac bypass surgery to

(cont. next page)

determine whether H rebound truly exists. Azure A levels of H were measured before the bypass procedure and every half hour from 0-8 hours after bypass in routine coronary artery bypass patients. Tests for prothrombin time (PT) and partial thromboplastin time (PTT) were performed simultaneously. The azure A test was performed on 252 samples of blood in the 27 patients; only one sample drawn anytime except immediately after bypass contained measurable H (0.4%). This sample became negative for H in the ensuing 30 minutes. In contrast, 12 of 27 patients had abnormal PTTs and 21 of 22 patients tested had abnormal PTs during the first 8 hours postoperatively, leading to the conclusion that 1) H rebound probably does not exist, or is at most, extr common postoperatively in the cardiovascular surgery patient who receives H and the tests do not predict the presence of H rebound; and 3) empiric doses of P are probably not justified in the postoperative period.

EMTAGS:

Therapy 0160; Adult 0018; Blood and hemopoietic system 0927; Clinical article 0152; Human 0888; Priority journal 0007; Diagnosis 0140

DRUG DESCRIPTORS:

\*heparin--drug therapy--dt; \*heparin--drug dose--do; \*protamine--drug therapy--dt; \*protamine--drug dose--do

MEDICAL DESCRIPTORS:

\*postoperative hemorrhage--drug therapy--dt; \*postoperative hemorrhage--complication--co; \*heart cannula--drug therapy--dt; \*blood clotting--diagnosis--di; \*azure a adult; prothrombin time; thromboplastin time

EMCLAS DRUG CODES:

03729010000; 03729000000

CAS REGISTRY NO.: 8057-48-5; 8065-01-8; 9005-48-5; 9005-49-6; 37187-54-5; 9007-31-2; 9012-00-4; 531-53-3

Record - 20

DIALOG(R) File 155:MEDLINE(R)

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06831733 89133733

The laboratory diagnosis of lupus anticoagulants [see comments]  
Lazarchick J; Kizer J  
Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston 29425.

Arch Pathol Lab Med (UNITED STATES) Feb 1989, 113 (2) p177-80, ISSN

0003-9985 Journal Code: 79Z

Comment in Arch Pathol Lab Med 1990 Jan;114(1):8-9

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 8905

Subfile: AIM; INDEX MEDICUS

With the well-documented association of lupus anticoagulants with thrombotic disease and recurrent spontaneous abortion, the laboratory approach to diagnosing these inhibitors is more critical now. To this end, we examined plasma samples from 21 patients who initially presented with a prolonged prothrombin time or activated partial thromboplastin time or both for the presence of lupus anticoagulants. We used a battery of coagulation tests, including both immediate and two-hour mixing studies, a platelet neutralization procedure, a tissue thromboplastin inhibition test, and dilute Russell viper venom times. Two patients (10%) had only a prolonged prothrombin time, seven (33%) had only a prolonged activated partial

(cont. next page)

thromboplastin time, and in 12 (57%) both were abnormal. In 15 patients, inhibition was evident on immediate assay of equal-volume mixture studies of patient plasma and normal pooled plasma, but in three additional patients it was evident only after a two-hour incubation. Fifteen of 18 samples showed correction of the abnormal screening study when platelets were used as a source of phospholipid. Both the tissue thromboplastin inhibition test and dilute Russell viper venom times were sensitive assays, being abnormal in 20 of 21 and 13 of 14 samples, respectively. In four patients, discordance of studies necessitated specific coagulation factor levels being measured to confirm the presence of the inhibitor. Because of the variable effect of the inhibitors on all currently available assay

procedures, we to have a battery of tests available before such an inhibitor can be excluded.

Tags: Human

Descriptors: \*Blood Coagulation Factors--Immunology--IM; Adolescence; Adult; Aged; Blood Coagulation Factors--Analysis--AN; Child; Child, Preschool; Diagnosis, Laboratory--Methods--MT; Middle Age; Partial Thromboplastin Time; Platelet Function Tests; Prothrombin Time; Thromboplastin--Antagonists and Inhibitors--AI

CAS Registry No.: 0 (Blood Coagulation Factors); 0 (Lupus Coagulation Inhibitor); 9035-58-9 (Thromboplastin)

#### Record - 21

DIALOG(R) File 155:MEDLINE(R)

(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

06451879 88096879

[Diagnostic usefulness and predictive value of laboratory tests in disseminated vascular coagulation]

Utilita diagnostica e valore predittivo di alcuni tests di laboratorio nella coagulazione intravasale disseminata.

Mori PG; Boeri E; Molinari AC; Odino S; Favareto F; Pecorara M; Arigliani R

IV Divisione Pediatrica, Istituto Giannina Gaslini, Genova, Italia.

Pediatr Med Chir (ITALY) Jul-Aug 1987, 9 (4) p469-72, ISSN 0391-5387

Journal Code: PAQ

Languages: ITALIAN Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE English Abstract

JOURNAL ANNOUNCEMENT: 8804

Subfile: INDEX MEDICUS

The laboratory tests of 38 patients in pediatric age with Disseminated Intravascular Coagulation (DIC) were retrospectively evaluated. In all patients were performed PT, aPTT, platelets count, FDP dosage and biological assay of Fibrinogen. In most of them the activity of FII, FV, FVII, FX and FVIII was assayed. According to the diagnostic criteria of FSP greater than 8 micrograms/ml, Platelets less than 150 10(9)/1 and Fibrinogen less than 150 ml/dl, in 16 patients the diagnosis of DIC was possible since first examination, while in 9 patients it became possible within 2-4 days; in 13 patients we never could diagnose DIC, although it was reasonably present, since the criteria above mentioned were never simultaneously satisfied. Looking back in our experience, we confirm that the platelets count and the quantitation of plasmatic Fibrin Degradation Products (FDP) are the most useful tests for the diagnosis of full blown DIC, and that the biological assay of plasmatic fibrinogen helps to follow the disorder. A low level of FVIII:C seems to be a forecast of failure. None of the other test performed give any useful information for diagnosis when it is not possible with the above mentioned tests.

(cont. next page)

Tags: Female; Human; Male  
Descriptors: \*Blood Coagulation Tests; \*Disseminated Intravascular  
Coagulation--Diagnosis--DI; Adolescence; Child; Child, Preschool;  
Disseminated Intravascular Coagulation--Physiopathology--PP; Partial  
Thromboplastin Time; Platelet Count; Prothrombin Time

Record - 22

DIALOG(R) File 73:EMBASE  
(c) 1994 Elsevier Science B.V. All rts. reserv.

6224669 EMBASE No: 86219732

Lupus anticoagulants: Improved diagnosis with a kaolin clotting time  
using rabbit brain phospholipid in standard and high concentrations

Rosove M.H.; Ismail M.; Koziol B.J.; et al.

Department of Medicine, University of California, Los Angeles, CA USA

BLOOD (USA), 1986, 68/2 (472-478) CODEN: BLOOA

LANGUAGES: ENGLISH

We utilized a kaolin-activated partial thromboplastin time (APTT) using  
rabbit brain phospholipid, in which the capacity of a fourfold increased  
'high' phospholipid concentration (PC) to normalize the abnormal 'standard'  
PC-APTT in patients with lupus anticoagulants is assessed. This system was  
also used to measure factors VIIIC, IX, and XI. The tissue thromboplastin  
inhibition test (TTI), a prothrombin time system in which the activity of a  
lupus anticoagulant is unmasked by the use of dilute thromboplastin, was  
simultaneously evaluated. Test sensitivity was defined by results on 31  
consecutive patients with standard PC-APTT inhibitors and no bleeding  
tendency. Specificity was based on 94 patients with various other  
coagulopathies, including coagulation factor inhibitors, severe congenital  
factor deficiencies, hepatic insufficiency, and warfarin and heparin  
treatment. Twenty-one patients with lupus erythematosus and standard  
PC-APTT results within normal limits were also tested. Sensitivity of the  
APTT system was superior to that of the TTI (97% v 58%); high PC normalized  
clotting time ratios and factor levels. Positive results were common with  
both assays in the group of 20 heparinized patients. The APTT system had  
superior specificity in remaining cases; there were no positive tests among  
74 patients. The lupus erythematosus group had a significant decrease in  
the clotting time ratio with high PC, indicating that low-level lupus  
anticoagulants are quite prevalent in this group. The kaolin clotting time  
using rabbit brain phospholipid in standard and high concentrations is a  
simple, sensitive, and specific technique for diagnosis of lupus  
anticoagulants.

EMTAGS:

Priority journal (0007); Methodology (0130); Immunological factors (0136);

Diagnosis (0140); Human (0888); Blood and hemopoietic system (0927);

Rabbits and hares (0731)

DESCRIPTORS:

\*systemic lupus erythematosus (0047331); \*kaolin agglutination test  
(0025210); \*partial thromboplastin time (0035968); \*anticoagulant agent  
(0002867); \*phospholipid (0037149)

lupus anticoagulant (0192522); diagnosis (0013133); rabbit (0040589);

phospholipid brain level (0006677)

SECTION HEADINGS:

02510050000 HEMATOLOGY/ BLOOD CLOTTING, FIBRINOLYSIS/ Thrombosis and  
embolism

02510030000 //Blood clot inhibiting factors

02521000000 /LABORATORY TECHNIQUES

02621020100 IMMUNOLOGY AND SEROLOGY/ AUTOIMMUNITY/ Clinical aspects/

(cont. next page)

Humoral immunity  
00618010000 INTERNAL MEDICINE/ CONNECTIVE TISSUE DISORDERS/ Lupus  
erythematosus  
00616140000 /HEMOPOIETIC SYSTEM/ Hemostasis and fibrinolysis  
01326010100 DERMATOLOGY AND VENEREOLOGY/ COLLAGEN DISEASES/ Lupus  
erythematosus/ Immunology  
03112040000 ARTHRITIS AND RHEUMATISM/ METABOLIC BONE AND JOINT DISORDERS/  
Clotting disorders  
03107010000 /CONNECTIVE TISSUE DISEASES/ Systemic lupus erythematosus  
03103010100 /BIOCHEMISTRY, PHARMACOLOGY AND PHYSIOLOGY/ Biochemistry/  
  
02907020000 CLINICAL BIOCHEMISTRY/ BODY CONSTITUENTS/ Plasma and serum  
09825000000 FIRST DECIMAL CLASSIFICATIONS/ HEMATOLOGY  
09826000000 /IMMUNOLOGY, SEROLOGY AND TRANSPLANTATION  
09806000000 /INTERNAL MEDICINE  
09813000000 /DERMATOLOGY AND VENEREOLOGY  
09831000000 /RHEUMATISM AND ARTHRITIS  
09829000000 /CLINICAL BIOCHEMISTRY

Blood

Record - 23

DIALOG(R) File 155:MEDLINE(R)  
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05586328 85202328

A clinical evaluation of automated chromogenic tests as substitutes for conventional prothrombin time and activated partial thromboplastin time tests.

Duncan A; Bowie EJ; Owen CA Jr; Fass DN

Clin Chem (UNITED STATES) Jun 1985, 31 (6) p853-5, ISSN 0009-9147

Journal Code: DBZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 8509

Subfile: INDEX MEDICUS

Automated procedures involving a chromogenic substrate sensitive to thrombin-sarcosine-Pro-Arg p-nitroanilide were compared with conventional tests for prothrombin times and activated partial thromboplastin times (APTT) and with specific assays for factors V, VII, VIII, IX, X, XI, and XII. The reproducibility and sensitivity of the chromogenic tests were compared with those of the clotting tests. Further, we have confirmed that the chromogenic test for APTT is sensitive to factor VII deficiency, unlike the clotting test for APTT. This might be an advantage in monitoring orally anticoagulated patients. The ready availability of the automated equipment for performing the chromogenic tests suggests their potential for routine use. However, some discrepant results in certain patients with liver disease and in others with factor VIII inhibitors warrant caution.

Tags: Human; Male

Descriptors: \*Autoanalysis; \*Blood Coagulation Tests; \*Chromogenic Compounds--Diagnostic Use--DU; \*Partial Thromboplastin Time; \*Prothrombin Time; Blood Coagulation Disorders--Blood--BL; Blood Coagulation Disorders--Diagnosis--DI

CAS Registry No.: 0 (Chromogenic Compounds)

Record - 24

DIALOG(R) File 5:BIOSIS PREVIEWS(R)  
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4448023 BIOSIS Number: 78021846

EFFECT OF TANSBINONE II-A SULFONATE ON THROMBUS FORMATION PLATELET AND  
COAGULATION IN RATS AND MICE

LI C-Z; YANG S-C; ZHAO F-D

DEP. PATHOPHYSIOL., FACULTY MED. SCI., SHANGHAI FIRST MED. COLL.,  
SHANGHAI 200032.

ACTA PHARMACOL SIN 5 (1). 1984. 39-42. CODEN: CYLPD

Full Journal Title: Acta Pharmacologica Sinica

Language: CHINESE

Tanshinone II-A sulfonate 12.5-38 mg/kg i.v. into rats and mice produced  
a prolongation of thrombus formation time, a shortening of thrombus length,  
a reduction of wet and dry thrombus weights, an inhibition of platelet  
adhesion and aggregation and prolongations of recalcification time,  
prothrombin time and kaolin partial thromboplastin time. Only platelet  
adhesion and aggregation were inhibited after i.v. 6.25 mg/kg in rats.  
These changes may be responsible for its clinical efficacy in treating  
angina pectoris.

Descriptors/Keywords: HUMAN APPLICATION ANTICOAGULANT CARDIOVASCULAR-DRUG  
ANGINA PECTORIS PROTHROMBIN TIME KAOLIN PARTIAL THROMBOPLASTIN TIME  
PHARMACODYNAMICS

Concept Codes:

- \*10808 Enzymes-Physiological Studies
- \*13012 Metabolism-Proteins, Peptides and Amino Acids
- \*14506 Cardiovascular System-Heart Pathology
- \*14508 Cardiovascular System-Blood Vessel Pathology
- \*15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph  
Studies
- \*15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
- \*15006 Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and  
Reticuloendothelial Pathologies
- \*22008 Pharmacology-Blood and Hematopoietic Agents
- \*22010 Pharmacology-Cardiovascular System
- 02506 Cytology and Cytochemistry-Animal
- 10060 Biochemical Studies-General
- 10064 Biochemical Studies-Proteins, Peptides and Amino Acids
- 10506 Biophysics-Molecular Properties and Macromolecules
- 10508 Biophysics-Membrane Phenomena
- 12504 Pathology, General and Miscellaneous-Diagnostic
- 12512 Pathology, General and Miscellaneous-Therapy (1971- )
- 14501 Cardiovascular System-General; Methods
- 22003 Pharmacology-Drug Metabolism; Metabolic Stimulators
- 22005 Pharmacology-Clinical Pharmacology (1972- )
- 22100 Routes of Immunization, Infection and Therapy
- 51522 Plant Physiology, Biochemistry and Biophysics-Chemical  
Constituents
- 54000 Pharmacognosy and Pharmaceutical Botany

Biosystematic Codes:

- 26515 Papaveraceae
- 86215 Hominidae
- 86375 Muridae

Super Taxa:

- Plants; Vascular Plants; Spermatophytes; Angiosperms; Dicots; Animals;
- Chordates; Vertebrates; Mammals; Primates; Humans; Nonhuman Vertebrates
- ; Nonhuman Mammals; Rodents

Record - 25

DIALOG(R) File 155:MEDLINE(R)

(cont. next page)

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04845024 83078024

Relation of simple clotting tests to clotting factor levels in liver disease.

Ruiz F; Grainger SL; Hall RJ; Ingram GI; Pollard V; Swan AV  
Clin Lab Haematol (ENGLAND) 1982, 4 (3) p247-56, ISSN 0141-9854

Journal Code: DKF

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 8304

Subfile: INDEX MEDICUS

The prothrombin time with Manchester and ox.thromboplastins, the 'P & P' test of Owren and Aas, the partial thromboplastin time, the thrombin time and assays for factors II, V, VII, VIII:C, IX and X were performed by one observer in 18 patients with liver disease and 27 normal subjects; the prothrombin time and partial thromboplastin time were also carried out on

another 28 si  
tests were measured in all patients. The prothrombin time with Manchester thromboplastin was well correlated with other clotting tests, and performing the other tests did not add to the information. Discriminant function analysis confirmed that clotting tests did not distinguish between different types of liver disease. Correlations between clotting tests and liver function tests reflected liver cell damage but were also influenced by acute phase reactions.

Tags: Human

Descriptors: \*Blood Coagulation Factors--Analysis--AN; \*Liver Diseases--Diagnosis--DI; Adolescence; Adult; Aged; Aging; Blood Coagulation Factors--Physiology--PH; Blood Coagulation Tests; Hepatitis, Chronic Active--Blood--BL; Hepatitis, Chronic Active--Diagnosis--DI; Liver Diseases--Blood--BL; Middle Age; Partial Thromboplastin Time; Prothrombin Time; Thrombin Time  
CAS Registry No.: 0 (Blood Coagulation Factors)

#### Record - 26

DIALOG(R) File 155:MEDLINE(R)

(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

04694248 82237248

Factor VII Padua 1. Another case.

Croze M; Brizard CP

Haemostasis (SWITZERLAND) 1982, 11 (3) p185-8, ISSN 0301-0147

Journal Code: FYG

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 8211

Subfile: INDEX MEDICUS

A patient with a peculiar factor VII is described. The propositus is a 70-year-old man without any bleeding tendency. The coagulation pattern is characterized by a prolonged rabbit brain prothrombin time, a normal Stypven cephalin clotting time and a normal thrombotest. Factor VII activity is low when assayed using rabbit brain the thromboplastin but is normal when assayed using ox brain thromboplastin. The neutralization test performed with an antifactor VII antiserum revealed a normal factor VII antigen level. A pedigree study has not been possible, the patient having no living relatives. No differences were observed between the biological results of our patient and those described by Girolami as factor VII + Padua.

Tags: Animal; Case Report; Human; Male

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Descriptors: \*Factor VII Deficiency--Blood--BL; Aged; Blood Coagulation Tests; Cattle; Factor VII--Genetics--GE; Factor VII--Immunology--IM; Factor VII Deficiency--Diagnosis--DI; Factor VII Deficiency--Genetics--GE; Prothrombin Time; Rabbits; Thromboplastin--Diagnostic Use--DU  
CAS Registry No.: 9001-25-6 (Factor VII); 9035-58-9 (Thromboplastin)

Record - 27

DIALOG(R) File 5:BIOSIS PREVIEWS(R)  
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3403548 BIOSIS Number: 72035939

1ST ARGENTINIAN THROMBOPLASTIN REFERENCE REAGENT FROM HUMAN BRAIN  
ARALDI H T; MARTINEZ CANAVERI A; LABERTENGO M E; CINTO R O; ELGUE

INST. INVEST. HEMAT

SANGRE (BARC) 25 (4). 1980 (RECD. 1981). 421-429. CODEN: SNGRA

Language: SPANISH

The 1st national thromboplastin reagent of Argentina (RNAT) was prepared from human brain. The tissue extract was included in 400 ampoules, and was later lyophilized and sealed in dry N atmosphere. The reagent was calibrated against the 1st international reference reagent of combined human thromboplastin (67/40) and the British Comparative Thromboplastin (BCT), following the recommendations of the 28th Report from the WHO Experts Committee on Biological Patterns. The results of the 1-stage prothrombin time performed in fresh plasma with coumarin were expressed as a quotient or ratio. Four Centers took part in the cooperative study. After evaluation of the results, the international calibration constant of the RNAT was 0.9, and the calibration constant against BCT was 1.1. In order to assess the effect of temperature on the normal values of prothrombin time and on the reagent's sensitivity to the coumarin-induced defects, samples were stored at 4, 37 and 50.degree. C. No significant differences were appreciated with regard to the reagent stored at -15.degree. C.

Concept Codes:

- \*10006 Clinical Biochemistry; General Methods and Applications
- \*10806 Enzymes-Chemical and Physical
- \*15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
- \*20504 Nervous System-Physiology and Biochemistry
- 10064 Biochemical Studies-Proteins, Peptides and Amino Acids
- 10614 External Effects-Temperature as a Primary Variable (1971- )
- 10616 External Effects-Temperature as a Primary Variable-Cold (1971- )
- 10804 Enzymes-Methods
- 23001 Temperature: Its Measurement, Effects and Regulation-General Measurement and Methods
- 23004 Temperature: Its Measurement, Effects and Regulation-Cryobiology

Biosystematic Codes:

86215 Hominidae

Super Taxa:

Animals; Chordates; Vertebrates; Mammals; Primates; Humans

Record - 28

DIALOG(R) File 155:MEDLINE(R)

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The varied sensitivity of partial thromboplastin and prothrombin time reagents in the demonstration of the lupus-like anticoagulant.

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Mannucci PM; Canciani MT; Mari D; Meucci P  
Scand J Haematol (DENMARK) May 1979, 22 (5) p423-32, ISSN 0036-553X  
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JOURNAL ANNOUNCEMENT: 7912  
Subfile: INDEX MEDICUS

An acquired inhibitor of blood coagulation, similar to that described in patients with Systemic Lupus Erythematosus (SLE), was detected during routine coagulation screening in 10 patients who did not meet the criteria for a diagnosis of SLE. The lupus-like anticoagulant (LLAC) was diagnosed on the basis and/or prothrombin time (PT) which failed to correct when patient plasma was added to normal plasma; an additional criterion was an abnormal tissue thromboplastin inhibition test. No patient had a specific inhibitor directed against factors VIII and IX. Demonstration of LLAC was highly dependent upon the type of reagents adopted in the APTT and PT: the abnormality was detected consistently by one reagent only. One-stage assays of factors VIII and IX were characteristic of the presence of an inhibitor, showing non-parallel dose-response curves or decreased activity at low dilutions which were partially corrected at higher dilutions. Although 7 patients were free of abnormal bleeding, unequivocal signs of haemorrhagic tendency after a surgery were present in the remaining 3 patients. The findings suggest that LLAC is a non-exceptional cause of prolonged coagulation screening tests, and that it may sometimes be associated with impaired haemostasis.

Tags: Female; Human; Male

Descriptors: \*Blood Coagulation; \*Blood Coagulation Tests; \*Lupus Erythematosus, Systemic--Blood--BL; Adolescence; Adult; Blood Cell Count; Blood Coagulation Factors--Analysis--AN; Blood Platelets; Child; Diagnosis, Differential; Lupus Erythematosus, Systemic--Diagnosis--DI; Middle Age; Prothrombin Time; Thromboplastin--Metabolism--ME